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THE RESULTS OF TREATMENT IN PERNICIOUS ANEMIA

By Arthur Bloomfield, M. D.

(From the Medical Clinic of The Johns Hopkins Hospital)

The treatment of pernicious anemia, generally employed until a few years ago, consisted of a regimen in which rest, special diet, and the administration of arsenic were the principal features. Recently more radical measures have come into prominence, namely, transfusion of blood, splenectomy, and operations for the elimination of "foci of infection." The reports on these newer methods have dealt so far mainly with general considerations and immediate results:

Ottenberg and Libman [1] state that transfusion leads to remission in about one-half of the cases. Archibald [2] found that of 26 patients who received transfusions 69 per cent derived marked immediate benefit. Larrabee [3] from a small experience (six cases), and Barker and Sprunt [4] feel that if the anemia is severe and progressive and responds poorly to other methods transfusion should be tried. Meleney and his associates,[5] without making detailed statements, conclude that transfusion is of real value in pernicious anemia, spontaneous remissions having been hastened in many cases by the procedure. With regard to splenectomy Lee, Vincent, and Robertson [6] found in a series of five cases that the immediate result was prompt post-operative recovery and a definite remission of the disease. Krumbhaar,[7] in a review of the late results of splenectomy in 153 cases, noted a post-operative mortality of about 20 per cent and also that the improvement was transient in most of the patients. Minot and Lee [8] emphasize the importance of careful selection of cases. Their report includes a thorough study of immediate and late results of transfusion and splenectomy in a somewhat larger series. They find that these measures, when properly employed, offer more than other methods of treatment alone, although they may fail in individual cases. A recent report by Giffin [9] states that splenectomy does not cure pernicious anemia but that there is considerable improvement in more than half of the cases, especially when the procedure is combined with transfusion. William Hunter first emphasized the relation of "oral sepsis" to severe anemias, and recently Barker and Sprunt [4] have laid stress on the importance of eliminating "foci of infection" in the treatment of pernicious anemia.

Inasmuch as these procedures are elaborate, and at times not without immediate ill effects, it seems important to have more information as to their value in prolonging life or inducing remissions. In this report a series of 57 cases has been analyzed in detail with particular reference to the comparative value of the various methods of treatment. All the patients were studied in the Medical Clinic of The Johns Hopkins Hospital and were selected serially from the records of the past five years. In every instance the history, physical findings, and the blood picture were typical of the so-called idiopathic type of pernicious anemia.

Determination of the value of therapy in this disease is notably difficult owing to certain features belonging to the natural course of the malady. The following possible criteria suggest themselves:

1. *The Effect of Treatment on the Total Duration of the Disease.*—This should be the most useful guide. It must be remembered, however, that the actual onset cannot be determined, and in only four-fifths of this series was there a clear history as to the beginning of symptoms. Furthermore, some of the cases run a rapidly progressive course, whereas others show repeated remissions. As a rule, the patient is under

close observation only during the relapses, and the care which he takes of himself at other times may influence the course of the disease. Thus the reappearance of symptoms has been noted not infrequently after exposure, shock, or over-exertion. Finally, the advantage of studying large series of hospital cases is to some extent offset by the difficulty of tracing many of these patients.

2. *The Readiness with which Remission is Induced.*—This furnishes a doubtful standard of treatment, since spontaneous remissions may occur at any time even when the blood count has been very low, or after the condition has been stationary under observation for several weeks or even months. Furthermore, remissions usually occur more readily in the earlier stages of the disease than later; in fact in every case there eventually comes a period when all measures are unavailing and the downward course is unarrested. This is illustrated by the cases of several patients in this series who returned to the hospital at intervals and finally became totally refractory to the measures that seemed before to produce striking results.

3. *The Length of the Remission.*—This is often difficult to determine. It may vary spontaneously, and depends to some extent on the conduct of the patient after leaving the immediate care of the physician.

4. *The Effect of a Particular Form of Therapy on Special Symptoms* is difficult to estimate.—Fever, gastro-intestinal disturbances, and the symptoms referable to the anemia itself tend to clear up as the remission sets in and the blood improves. The spinal cord disturbances on the other hand are notably but little affected by any therapy, and may even progress at a time when the condition seems to be improving in other ways. Gain in weight does not always run parallel with improvement in the blood count and general condition. The degree of the remission, with reference to the gain in blood, may furnish some standard of the effect of therapy.

5. *The death rate in the hospital* offers a means of comparing the value of therapeutic measures, but often the patient is in a late stage of the disease refractory to any treatment.

6. *The Character of the Blood Picture.*—Minot and Lee[8] recently report morphological blood studies in pernicious anemia which may turn out to be of aid in prognosis and in estimating therapeutic effect, but since gain or loss of blood elements depends on the balance of blood destruction and blood formation, patients showing the most active signs of regeneration may be doing badly, whereas others may gain rapidly without evidence in the peripheral blood of marked marrow stimulation.

Very little information is at hand about the immediate effect of transfusion or splenectomy on the blood picture. Lee, Minot and Vincent[10] find immediate stimulation of the bone marrow following splenectomy, and Meleney[8] has noted a leucocytosis shortly after transfusion.

It is clear that no single standard of therapeutic effect is reliable. In this report, therefore, the cases have been analyzed from these various points of view.

Results of General Treatment

Twenty-eight cases were treated by the older methods consisting essentially of rest in bed, diet, hydrochloric acid, and arsenic. The results of such therapy are well known and these patients are included mainly as controls to compare with those who had transfusion or splenectomy, or in whom foci of infection were eliminated. A few points may, however, be emphasized. Absolute rest in bed over considerable periods of time is certainly the most important feature of this regimen. Arsenic and hydrochloric acid are apparently useless, unless the patient is kept quiet at the same time, and cessation of improvement or relapse has occurred not uncommonly as soon as active life was resumed, despite continued drug therapy. Furthermore, it often appears on going back into the history of the period of the disease before the patient was under medical care that the "weakness and shortness of breath" were relieved by a few weeks of rest in bed. The value of arsenic is based entirely on general impressions. It was used in every instance in this series either in the form of Fowler's solution, sodium cacodylate, or salvarsan. Analysis of the cases, however, yields no data of value as to its efficacy. Achlorhydria gastrica was uniformly present and hydrochloric acid was given usually both before and after meals. In a few instances gastro-intestinal disturbances, especially diarrhœa, seemed to be relieved, but in most of the patients these symptoms disappeared quite rapidly with the progress of the remission apparently regardless of any symptomatic therapy. In about one-half of the cases there were accurate statements as to loss of weight. This usually amounted to from 10 to 50 pounds from the onset of symptoms to the time of admission to the hospital. Unless special features of the case made feeding impossible, a liberal diet was allowed. No special dietary regimen or restriction of any food element was attempted. No relation between gain in weight and improvement in the blood or general condition is apparent in this series. Of 33 cases in which there was clinical improvement, and the weight on admission and discharge was recorded, 22 gained and 11 lost. The examples in Table I illustrate that gain in blood does not

TABLE I

Patient	Blood count on admission	%	Blood count on discharge	%	Days in hospital	Weight on admission in pounds	Weight on discharge in pounds	Loss in pounds
Hu...	2,400,000	50	3,300,000	76	78	151	135	16
H.....	1,300,000	20	3,400,000	60	40	133	127	6
B.....	1,100,000	27	4,000,000	62	51	130	118	12
P.....	1,130,000	26	3,400,000	60	48	174	164	10
G.....	1,400,000	43	3,000,000	60	35	91	81	10
S.....	800,000	22	2,200,000	47	85	93	91	2

necessarily go hand in hand with gain in weight. After a remission is established and digestive disturbances have cleared up, rapid gain in weight usually occurs.

Transfusion

Twenty-six patients received transfusions of blood varying in number from 1 to 17. The largest amount of blood given to one patient was 8700 cc., the smallest amount was 300 cc. The

single transfusions varied in amount from 300 to 900 cc. The citrate method and the Lindeman syringe method were used most often; in a few cases indirect transfusions of defibrinated blood were given, and in one case direct transfusion was used as a preliminary to splenectomy. The technique employed has been described recently by McClure and Dunn,[11] and by Sydenstricker, Mason and Rivers [12] from this clinic, and will not be repeated.

The therapeutic effect of transfusion in pernicious anemia may be discussed under several heads.

1. *The Value of Transfusion as an Emergency Measure.*—Quite apart from any ultimate effect the question arises whether transfusion may tide over a patient during an unusually severe relapse, or may check further fall of the blood count where this is very low. To illuminate this point the following mortality statistics are presented. Three hundred and sixty-three patients with pernicious anemia have been treated in The Johns Hopkins Hospital, of whom 58, or 16 per cent, died in the wards. Of the 31 who received transfusion 6, or 19 per cent, died, whereas of the 332 who did not receive transfusion 52, or 15.5 per cent, died. Of the 57 cases studied in this report, 26 were given transfusions with 6 deaths in the hospital—23 per cent. Of the 22 cases not transfused and receiving only general therapy, 5, or 22.7 per cent, died. Some of the patients were admitted to the hospital several times. The patients who were given transfusions had 37 admissions with 6 deaths, or 16.2 per cent; those not transfused had 28 admissions with 5 deaths, or 17.8 per cent. The cases have been divided further into those entering with counts of less than 1,000,000 red cells, and those with counts of over 1,000,000 red cells. Patients not receiving transfusion were admitted 10 times with counts of less than 1,000,000, and 18 times with counts of over 1,000,000. Two of the former—20 per cent—died; 3 of the latter, or 17 per cent. Of the 37 receiving transfusions 9 entered with counts of under 1,000,000 of whom 3, or 33.3 per cent, died; of the 28 with counts over 1,000,000, 3, or 33.3 per cent, died; of the 28 with counts over 1,000,000, 3, or 10.7 per cent, died.

These figures, therefore (Table II), furnish no evidence that transfusion was of value as an emergency measure, or that the immediate mortality was decreased by the procedure.

TABLE II

	Cases receiving transfusion			Cases not receiving transfusion		
		Deaths			Deaths	
	Number	Number	Per cent	Number	Number	Per cent
Total cases	26	6	23.0	22	5	22.7
Total admissions	37	6	16.2	28	5	17.8
Cases with counts under 1,000,000	9	3	33.3	10	2	20.0
Cases with counts over 1 000,000	28	3	10.7	18	3	17.0

2. *The Immediate Effect of Transfusion.*—Following the injection of 500 cc. or more of blood there was usually an immediate increase in the blood count and hemoglobin. Rises of as much as 1,000,000 cells and 15 per cent of hemoglobin were frequently noted. In most cases there was a subsequent fall. Counts were not made often enough to distinguish the purely mechanical result of transfusion from later reactive effects. This question is now being studied in detail. Subjective improvement was often striking, the patient saying he felt better while the blood was being injected. Quite possibly this was in some cases a psychic effect.

3. *The Relation of the Onset and Degree of Remission to Transfusion.*—The cases were studied to find out if remission occurred sooner and more often in patients receiving transfusion than in others. For the purpose of this discussion a remission is regarded as including marked general and symptomatic improvement with a gain of at least 1,000,000 red cells or 20 per cent of hemoglobin. Among the patients who were not transfused remission set in in the hospital 8 times in 28 admissions, a percentage of 28.5; in the patients given transfusion there were 19 remissions in 37 admissions, or 51 per cent. The number of days in the hospital until the highest blood count was reached averaged 43 in the untransfused patients, and 43 in those receiving blood. The maximal count was reached on an average of 34 days after the first transfusion.

The degree of the remission as measured by gain in blood was also studied in the two groups. Counts of 4,000,000 or over were reached in 4 cases of the group receiving blood, counts of 3,000,000 to 4,000,000 in 9, and counts of 2,000,000 to 3,000,000 in the remaining 6. Counts of 4,000,000 or over were reached only once in the patients who were not transfused, counts of 3,000,000 to 4,000,000, only twice, the remaining 5 patients reaching counts of from 2,000,000 to 3,000,000. Gains of over 3,000,000 cells were made in 4 patients receiving transfusion, gains of 2,000,000 to 3,000,000 in 6, and gains of 1,000,000 to 2,000,000 in 9. The largest gain in the patients who were not transfused was 3,000,000 in one instance, another gained 2,000,000 cells, 4 gained from 1,000,000 to 2,000,000 cells, and 2 gained less than 1,000,000 cells and but 22 per cent and 30 per cent of hemoglobin respectively. These facts are summarized in Table III.

TABLE III

Patients receiving transfusion				Patients not receiving transfusion			
Number of admissions	Remissions			Number of admissions	Remissions		
	Number	Per cent	Days		Number	Per cent	Days
37	19	51	43	28	8	28.5	43
Reaching counts of	Number	Per cent		Reaching counts of	Number	Per cent	
4,000,000 or over	4	21		4,000,000 or over	1	12.5	
3,000,000 to 4,000,000	9	47		3,000,000 to 4,000,000	2	25.0	
2,000,000 to 3,000,000	6	32		2,000,000 to 3,000,000	5	62.5	
Gains of	Number	Per cent		Gains of	Number	Per cent	
3,000,000 or over	4	21		3,000,000 or over	1	12.5	
2,000,000 to 3,000,000	6	32		2,000,000 to 3.000,000	1	12.5	
1,000,000 to 2,000,000	9	47		1,000,000 to 2,000,000 or 20% Hb.	6	75.0	

The relation of gain in blood to the amount of blood given is shown in Table IV.

TABLE IV

Patient and number of admission	Number of transfusions	Amount of blood given c. c.	Gain in blood (R. B. C.)	Days from admission	Days from first transfusion	Duration of symptoms on admission (approxim.)
B. 1.....	5	4400	3,000,000	38	23	10 mos.
P. 1.....	6	3120	3,500,000	37	29	12 "
Pr. 1....	6	2980	2,200,000	34	25	12 "
P. 3.....	6	2850	2,300,000	43	38	18 "
H. 1.....	5	2770	1,400,000	36	26	?
B. 2.....	3	2500	2,300,000	13	9	12 "
Bu. 1....	5	2300	1,500,000	34	24	12 "
Bu. 2....	5	2220	2,100,000	27	23	18 "
S.....	4	1650	1,400,000	83	73	12 "
E.....	4	1500	3,000,000	35	34	?
M. 1.....	3	1500	2,200,000	31	29	12 "
A. 1.....	2	1450	1,000,000	52	47	9 "
Bu. 3....	4	1400	1,100,000	31	25	24 "
Pr. 2....	3	1325	900,000	93	91	24 "
Mur.....	3	1300	600,000	132	88	3 yrs. ?
S. 1.....	4	1160	1,600,000	35	25	?
M. 2.....	3	1150	400,000	35	33	18 mos.
O.....	3	920	500,000	60	58	24 "
H.....	2	800	2,100,000	40	33	8 "
W.....	1	750	300,000	17	3	?
Bre.....	1	650	100,000	45	1	?
M.....	1	630	400,000	23	4	8 "
Bi.....	2	600	3,300,000	90	89	1 "
C.....	2	550	1,800,000	42	35	?
Wad.....	1	375	1,000,000	56	37	12 "
Be.....	1	250	600,000	36	29	8 "
H. 2.....	5	3500	Died, second. lues, pneumonia.			?
B. 3.....	3	1600	Died, coma.			18 "
Horn....	3	1000	Died, coma.			48 "
P. 4.....	3	420	Died, coma.			24 "
Ha.....	1	300	Died, coma.			8 "
Mu.....	1	300	Died, edema of lungs.			12 "

From this table it appears that the patients receiving most blood in general made the greatest gains. Thus, of the 10 gaining 2,000,000 or more cells, 8 received 3 or more transfusions with a total of 1500 cc. or more of blood. None of the 5 receiving only one transfusion of less than 1000 cc. gained over 1,000,000 cells. Of the 19 cases regarded as having a remission all but one received more than one transfusion and all but 5 received 1400 cc. or more of blood.

The success of transfusion seems to depend also on the stage of the disease. Where the previous duration of symptoms could be clearly determined in the patients showing a remission it was found to be 12 months or less in 10 instances, 18 months in 2, and 24 months in 1 case. The importance of the stage of the disease is further illustrated by transfusion results in the same patients on repeated admissions to the hospital (Table V).

In summary, then, it seems that in patients who are not in a stage of the disease refractory to any form of treatment, remission has come on more often when transfusion has been performed. Furthermore, the amount of blood gained runs roughly parallel to the number of transfusions and the total amount of blood given. It seems rational, therefore, if transfusion is done at all, to be prepared to inject blood repeatedly if the patient shows a tendency to respond. Single transfusions in cases refractory to other therapy led to no improvement in this series.

4. *The Length of the Remission.*—It was possible to determine accurately the length of the remission following transfusion in 13 instances. The return of symptoms with a fall in the blood count was regarded as indicating the onset of relapse. These data are summarized in Table VI.

TABLE V

Patient and number of admission	Number of transfusions	Amount of blood given c. c.	Gain in blood (R. B. C.)	Days from admission	Days from first transfusion	Duration of symptoms on admission (approxim.)
B. 1....	5	4400	3,000,000	38	23	10 mos.
*B. 2....	3	2500	2,300,000	13	9	12 "
B. 3....	3	1600 severe reactions to homologous blood; death.				18 "
*P. 1....	6	3150	3,500,000	37	29	12 "
P. 2....	5	2300	800,000 (34% Hb.)	49	47	14 "
P. 3....	6	2850	2,300,000	43	38	18 "
P. 4....	3	420 severe reactions to homologous blood; death.				24 "
Bu. 1...	5	2300	1,500,000	34	24	12 "
Bu. 2...	5	2200	2,100,000	27	23	18 "
Bu. 3...	4	1400	1,100,000	31	25	24 "
M. 1....	3	1500	2,200,000	31	29	12 "
M. 2....	3	1150	400,000	35	33	18 "
Pr. 1....	6	2980	2,200,000	34	25	12 "
Pr. 2....	3	1325	900,000	93	91	24 "

* Splenectomy.

TABLE VI

Patient and number of admission	Amou t of blood given c. c.	Duration of symptoms at time of remission	Duration of remission	Previous remissions	Subsequent remissions
B. 1.....	4400	10 mos.	2 wks.	0	
Pr. 1 ...	2980	12 "	10 mos.	0?	1
Bu. 1....	2300	12 "	6 wks.	0	3
Bu. 2....	2200	18 "	4 mos.	1	2
Bu. 3....	1400	24 "	4 wks.	2	1
Bu. 4....	1500?	28 "	4 wks.	3	0
M. 1.....	1500	12 "	4½ mos.	2	0
A. 1.....	1450	9 "	2½ "	0	
Pr. 2....	1325	24 "	4 " +	1	
G.....	1160	?	20 " +	0	
H.....	800	6 "	7 "	0	0
C.....	600	3 yrs.	5 "	?	0
Bi.....	550	2 wks.	8 "	0	0

These cases do not indicate that transfusion led to prolongation of the remission. In only three instances did it last over six months, whereas among 329 cases collected by Cabot [12] there were remissions of over six months in 165. No relation between the amount of blood given and the duration of the remission is apparent.

5. *The Duration of Life.*—Thirteen of the patients receiving transfusion are now dead, four are alive, while the remainder could not be traced. The total individual duration of life from the onset of symptoms was as shown in Table VII.

Although this series is too small to serve as a basis for group percentages it is clear that there was no demonstrable prolongation of life in the cases in which transfusion was employed. Patients treated by the older general methods frequently live four years or longer. Thus, in 647 cases Cabot [12] found 79 patients who lived over four years. Furthermore, it is noteworthy in this series that the patients living longest were not the ones in whom remission followed transfusion.

Four patients are still alive. The symptoms have been present one, two, two, and four years respectively.

TABLE VII

Patient	Duration of life from onset of symptoms	Remission after transfusion
H.	4 yrs.	None.
W.	4 "	None.
H.	3½ "	None.
C.	3½ "	Remission.
O.	3½ "	Remission.
M.	2 "	Remission.
D.	1½ "	None.
H.	1½ "	Remission.
M.	1½ "	Remission.
B.	1 "	Remission.
M.	1 "	None.
M.	10 mos.	None.
H.	8 "	None.

6. *The Effect of Transfusion on Symptoms.*—An analysis of the course of symptoms shows no definite variation in the groups of cases treated by different methods. In general, with the improvement in the blood, the symptoms referable to the anemia itself (dyspnœa, palpitation, dizziness, and weakness), and the gastro-intestinal disturbances were alleviated or disappeared. Fever regularly tended to fall and was rarely present on discharge in the patients who did well otherwise. Absence of relief of the central nervous system symptoms during the remission is well known. It was striking that transfusion also was ineffective in removing these disturbances. The disappointment of the patients was uniform in this regard, although in a few instances there was perhaps slight improvement.

SPLENECTOMY

Although splenectomy for pernicious anemia is no longer done in this clinic, it seems of interest to report the late results. The operation was performed in 8 instances. In one, death from pulmonary embolus occurred 19 days after operation. Six of the remaining patients are dead. The data in these cases are summarized in Table VIII.

In no case was the clinical picture essentially altered, and no unusual prolongation of life occurred. Thus one patient lived two and a half years after splenectomy, and another is alive after one and a half years but very ill with recurring femoral phlebitis. In five cases transfusions were given during the period immediately following splenectomy. None the less in the four cases in which the length of the remission could be accurately determined symptoms returned after periods of three, four, four, and eight months, respectively. In one case there was no remission but progressive failure, in another postoperative death occurred from pulmonary embolus. The other two patients did not have the relapsing type of the disease. The height of the blood count cannot be regarded as remarkable, inasmuch as the patients were transfused after operation except those not of the relapsing type. These cases fail to bear out the view that transfusions are " held " better after splenectomy. In the four cases in which 4000, 5200, 2300 and 3000 cc. were given, the blood was not " held " at all by one patient, and in the others symptoms returned after three, three and four months, respectively. All these patients reacted to trahsfusion in essentially the same manner before splenectomy was done. Three patients showed marked spinal cord symptoms. In B., who had no marked anemia, " the spinal sclerosis progressed rapidly, although the blood was about stationary until very near the end." In P. the cord changes progressed rapidly. Four months after operation he was unable to walk without crutches. Patient S. was admitted with absent knee-jerks, marked ataxia, and impaired muscle sense. The blood count was 2,260,000, 3200, with 43 per cent Hb. After two months the count was 3,100,000, 3000, with 87 per cent Hb., all the symptoms had cleared up, there were no paræsthesias, and the knee-jerks were obtained. The treatment had consisted of

TABLE VIII

Patient	Age	Duration of symptoms at time of splenectomy	Blood at time of splenectomy			Previous remissions	Previous transfusions		Maximal blood count after splenectomy			Days	Length of remission	Transfusion after splenectomy		Total duration of life from onset of symptoms	Duration of life after splenectomy	Remarks
					%		No.	c. c.			%			No.	c. c.			
W..	35	1 year.	1,700,000	3,600	27	?	1	375	3,500,000	10,400	70	60	8 mos.	*	*	4½ yrs.	2½ yrs.	Three subsequent remissions. Death from acute dysentery.
P...	62	1 "	4,000,000	1,400	65	1	6	3120	4,700,000	4,600	84	32	8 "	11	5200	2 "	11 mos.	Rapidly progressive cord changes. Death in coma.
B...	43	8 mos.	3,400,000	.....	60	1	8	5988	3,800,000	6,000	72	42	3 "	5	2300	19 mos.	7 "	Death in coma.
A...	38	14 "	1,800,000	3,000	35	1	5	3475	4,900,000	4,900	90	74	4 "	7	5000	2½ yrs.	16 "	Death in coma after rapid relapse.
Bo.	55	10 "	2,800,000	5,300	93	?	0	....	3,900,000	6,800	100	45	Disease not of relapsing type.	1	400	29 mos.	19 "	Progressive cord changes. Death in coma after rapid relapse.
S...	25	1½ yrs.?	3,100,000	3,000	87	?	0	....	4,200,000	8,400	102	..	Disease not of relapsing type.	0	....	3 yrs. (alive)	1½ yrs. (alive)	Patient still living.
H..	57	3 "	2,9 0,000	10,400	58	?	5	2770	2,100,000	.....	34	..	No remission.	6	4000	3½ yrs.	5 mos.	Rapidly progressive anemia. Pneumonia, death.
C..	42	5 mos.	3,500,000	7,000	91	?	0	....	.....	.....	...	..	.....	0	....	6 mos.	20 dys.	Death, pulmonary embolus.

* Direct transfusion at time of splenectomy

rest, diet, arsenic, and hydrochloric acid. Splenectomy was then performed. This patient's blood has remained fairly high ever since. He is alive after one and a half years.

In summary, these cases furnish no proof that life was prolonged, that remission was longer and more marked, that transfusions were better "held," or that there was any special relief of symptoms following splenectomy.

Elimination of "Focal Infections"

Since the work of William Hunter, many writers have ascribed the picture of pernicious anemia to local "foci of infection." This doctrine has come especially to the front in the last few years largely owing to the studies of Billings[14] and his co-workers. That the association of these foci with pernicious anemia is a causal one is not, however, as yet proved. It seems that one should be very cautious in assuming an etiological relationship between a disease picture so clear cut and running such a typical course as pernicious anemia and lesions of such frequent occurrence as periapical abscesses, infected tonsils, and other local "foci of infection." The anemias known to be due to infection such as those occurring in septic diseases are of the simple secondary type and clear up when the primary disease heals or is eliminated. It may be that less definite deleterious effects are exercised on the course of the disease by foci of infection without specific causal relationship.

In 12 cases a thorough study of the nose, throat, sinuses, teeth, gastro-intestinal tract, and lower urinary tract was made for foci of infection and, when found, these were eliminated. All these patients finally received clean bills of health from the various specialists. Most of them were given transfusions and in one case splenectomy was also performed. In none was there any feature in the subsequent course to distinguish them from the group in which foci were not found, or if found were not treated, either as to total duration of life or extent and degree of remission.

It is unlikely, therefore, that such foci of infection are the cause of pernicious anemia, although it seems wise to treat them for their own sake as well as for any possible general beneficial effects which may follow.

Conclusions

An effort has been made to analyze the results of treatment in these cases from a purely objective point of view. Clinical impressions have been disregarded, and no attempt has been made to promote or discredit any particular therapeutic measure. It should be recognized that such statistics lead to only general conclusions which allow of exceptions in individual cases. The results may be summarized as follows:

1. No definite evidence has been found that either transfusion, splenectomy, or elimination of foci of infection prolongs the life of patients suffering from pernicious anemia.

2. Transfusion performed at a time when the patient was not refractory brought on remission in about half the cases, and enabled the blood count to be raised to a higher level than it reaches in cases not so treated.

3. Such artificial plethoras did not increase the duration of the remission, although the patients usually had a sense of well being while the count was high.

4. At other times the same patients were refractory to transfusion as well as to other methods of treatment.

5. The central nervous system symptoms were as little benefited by transfusion and splenectomy as by other methods of therapy.

6. Transfusions of blood were not "held" better after splenectomy than before.

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TOBACCO SMOKE AND PULMONARY TUBERCULOSIS*

By Allen K. Krause

This study[1] may strike many as having turned out "against the rule." But to some of us its results are not unexpected. Major Webb finds, in effect, that comparatively few non-smokers (only 27 per cent) have ronchi, while most smokers do exhibit these signs of chronic bronchial irritation, and cigarette smoke inhalers almost invariably show them (83 per cent). He finds further that of a comparatively large body of young men (over 3000), the proportion that was discharged from active army service because of active tuberculosis was no higher among the smokers, the men who had ronchi, than among the non-smokers with relatively "quiet" chests.

* Elaboration of remarks made in a discussion of a paper, "The Effect of the Inhalation of Cigarette Smoke on the Lungs. A Clinical Study," read by Major Gerald B. Webb before the Laennec Society of The Johns Hopkins Hospital, February 25, 1918.

Ronchi are indications of bronchial irritation and a consequent inflammation; and it might have been predicted that individuals who are habitually subjecting their respiratory tract to the far-from-soothing influence of cigarette smoke would be more likely to exhibit its effects, that is, inflammation, than those whose gaseous intake is confined to the more or less undefiled atmospheric air of town and country. This side of Major Webb's study represents, therefore, no startling discovery. But its other result—that the "ronchous" smoker's acquaintance with the tubercle bacillus is just as favorable and just as well guarded as that of his non-smoking neighbor—embodies certain implications that run so counter to what we have been taught and what we have comfortably believed, that it perhaps deserves a little more than a word of notice.

We were once told that in our struggle against the tubercle bacillus it was of great importance that we avoid anything that would bring about irritation of the respiratory tract. I believe that much of the antituberculosis propaganda still recites that inflamed conditions of the nose, throat, larynx and bronchi lay us more open to tuberculous infection. The old admonitions had it that the inflammations brought about by the common cold, catarrh, tobacco, etc., left us in a "run down" condition and therefore comparatively defenseless against bacillary invasion. The idea undoubtedly had its birth in the long-noted and indisputable fact that the common cold and other catarrhal conditions were frequently followed by outbreaks of pulmonary tuberculosis. Therefore, the local inflammation was favorable and nourishing soil for the implantation of tubercle bacilli and a host of other microörganisms. This was a very natural presumption. For an inflamed tissue is a diseased tissue and without examining the matter more closely it seems reasonable to presuppose that a diseased tissue is more open to infection—to bacterial implantation and invasion—than a healthy tissue.

But let us analyze these matters further. In another place I[2] have already pointed out that it is at least debatable whether inflammation leads to increased susceptibility to bacterial infection. Clinical data at once belie this assumption. If the proposition is maintained, then I would at once ask questions something as follows: Why are chronic leg ulcers so uncommonly the seat of acute bacterial infection? Why is erysipelas more often seen to arise in the healthy non-inflamed skin or in the clean, operative wound than in the epithelioma ulcer or in the open patch of lupus where we should look for it? Why is a story of frank, acute bronchitis ushering in acute lobar pneumonia unusual?

In this connection too I have elsewhere called attention to what Opie[3] has to say on the function of inflammation. "Views concerning the nature of inflammation," he writes, "are widely diverse, but all are agreed that inflammation accomplishes the destruction and solution of a variety of substances, and notably those proteins which form the bodies of parasitic invaders." In the same lecture Opie cites experimental evidence as follows: "Pawlowsky has demonstrated the presence of staphylococci in the blood and organs of guinea-pigs from 24 to 48 hours after inoculation of the knee-joint, but has been able to show that dissemination is inhibited or wholly prevented if, before inoculation, acute inflammation of the joint has been produced by the injection of some sterile irritant, such as turpentine, alcohol or solution of quinine." And again, "Issayeff . . . . showed that the peritonitis induced by a variety of sterile irritants, such as a foreign blood serum, bouillon, or normal salt solution, temporarily increases resistance to subsequent intraperitoneal inoculation of bacteria."

Now what does all this mean? It must at least suggest that inflammation is the visible expression of an animal organism's capacity to react to irritation (whether the irritation be mechanical, chemical or thermal; whether it be set up by organized or unorganized material, by inert or living substances, by grains of sand or bacterial parasites), and that this reacting capacity is a true resisting function of tissues. It is an effort on the part of tissue to defend itself, to limit the assault of the invader, to wall off the offending irritant. If this be true—and to me it hardly admits of any doubt—we must give up our ideas that inflamed tissues are especially favorable soil for bacterial invasion. They are the very reverse: they are points of unusual resistance.

It would be perfectly useless to speculate as to what element in the inflammatory process brings into the struggle the resisting units or substances—as to whether the serum, or the leucocytes, or the new proliferation of fixed cells renders the invaders impotent. That is material for studies of another nature. The point I want to make here is that the animal body interposes a something, a barrier, if you will, between itself and parasites that are trying to gain a foothold; and that the subsequent fate of the animal will depend largely on the competence and integrity of this barrier. In what this competence consists is another matter that is not at present germane.

It is because of considerations like these that some of us have begun to doubt the soundness of the view that looks upon an inflamed spot as a *locus minoris resistentiæ* for infection by microörganisms. But what we have to say applies only to the incident of *becoming infected*, not to what may or may not happen to a focus of infection that is already established.

It seems to me that it is not sufficiently well recognized, or, at least, not emphasized enough, that the factors that favor or prevent the implantation of an infection need not be at all similar to those that favor or prevent the spread of an infection, once it has taken place. This point is beautifully illustrated in an infection that tends to focalize like tuberculosis. In general, we can say that relative stasis is favorable to infection, but less likely to promote the spread of tubercle, while relative movement is likely to prevent localization of bacilli, but more prone to spread tubercle once the bacilli have focalized; that is, other factors like the numbers of bacilli and the character of the respective tubercles being equal. We find, therefore, that infection of the lung with tubercle bacilli is much more common at the apex where movement (of lung, of air current and of lymphatic flow) is relatively small, than lower down and towards the front where movements are comparatively great. It is the rule for first infections to occur toward the tops and

posterior surfaces where movements are relatively restricted by less yielding structures, as compared with the more expansile front and bottom of the thoracic cage. Similarly, pleural adhesions are in general much more abundant and of much greater extent above and in back than in front and below; and when they do occur in front and below they are likely to be attached to the ribs which are more fixed than the intercostal spaces.

Now, though first infection prefers the top and back of the lung, the tubercle that results therefrom is much more likely to reach quiescence and arrest than if infection takes place in the more movable parts of the lung. Even when tubercle formation has become extensive we become much more concerned about the formation of what we might call mid-pulmonary disease than about the same amount of apical disease. Clinical experience has taught us that in the former case we are dealing with a more serious condition than in the latter; and one of the reasons for this is that, as compared with relative inactivity, movement favors the mobilization and spread of focal products.

I have touched on this matter of the effects of movement and inactivity on two contrasting and different phases of tuberculosis, namely, infection and metastasis, because I want to protest against the confusion that usually involves any discussion of tuberculosis, when, as generally happens, it is assumed that what holds good in reference to the taking place of infection also holds as concerns its further development and spread, and when, as so often happens, the factors that govern therapy are mixed up or made identical with those that relate to prophylaxis. And I am further desirous of pointing out how inflammation can have two very different effects, depending on whether it is concerned with implantation of bacilli or an action on a focus already present.

As regards implantation, my argument has already laid it down that microörganisms that are brought to a tissue that is already inflamed fall on relatively resistant soil. But as regards the further development and spread of an already established focus, inflammation can exert an effect that may not be so favorable. Tubercle anywhere in the body is benign or innocuous just so long as its investing envelope is of such a nature that it is so impervious to the circulation of tissue juices that goes on between it and the host that the maximum amount of material absorbed is not enough to produce symptoms of intoxication in the host and the maximum of the kinetic energy of the circulation is not sufficient to mobilize bacilli and spread them. As sclerosis of tubercle proceeds, the interior of the formation becomes more and more shut off from the surrounding tissues. Now, anything that can bring about a better circulation around this avascular structure, anything that will promote an enhanced give and take between it and the surrounding tissue, will tend to "unlock" or "open up" this walled-in structure. Among other things this is exactly what inflammation—hyperæmia, congestion, etc.—can do and frequently does do. And when it does this then inflammation becomes a contributory and inciting factor to the development of tuberculosis: not, remember, to infection with tubercle, but to the spread of tubercle, or the development of tuberculosis. Here then we can look upon inflammation as we viewed movement—as capable of exerting two very different and antithetical effects, depending on whether we are considering either of two very different phases of what in the large is one problem.

Let us now come back to Major Webb's paper and the immediate questions that its subject matter raises. Major Webb finds that men with bronchi in a state of chronic inflammation do not develop the disease tuberculosis in larger proportions than men with what might be called more normal bronchi. The older view was that inflammations of the respiratory tract do predispose to tuberculosis, and I believe that many assumed that this predisposition was a predisposition to infection. To-day, with our newer knowledge of the relative incidence of infection and morbidity, few of us, even without going into the matter further, would believe that, if men with inflamed throats and bronchi fell ill with tuberculosis, this disease was the result of recent infection. We should be more inclined to believe that the disease represented the awakening of old quiescent tubercle, planted perhaps years before. Therefore, on this basis alone, we should say that irritation of the upper respiratory tract in an adult played no part in infection. But we have in addition pointed out that inflammation, if it does anything, probably resists a fresh infection.

Now, if it were granted that inflammation does not lay a tissue more open to infection, but that on the contrary it probably plays a part in resisting bacterial invasion, it still remains for us to consider what effect constant irritation, brought about perhaps by some such stimulus as tobacco smoke, might have on foci of tubercle that exist in tissue. This set of circumstances would no doubt represent what more likely occurs under natural conditions; that is, some tubercle is already present in the lungs of individuals who take up the smoking and inhaling habit, and it is this tubercle that later blazes out into clinical disease, and again, therefore, it is this tubercle on which the inhaled cigarette smoke exerts an effect.

It will immediately occur to every one that if nearly everybody has quiescent tubercle and if inflammation can exert an awakening influence on such dormant tubercle and if frequently the ultimate result of the inhalation of cigarette smoke is a chronic bronchial inflammation, then why do not more cigarette inhalers develop tuberculosis? The answer is, that the factors are not so simple as this qualitative statement of the problem. To go a little further we must deal with the quantitative phases of the situation.

It is not to be doubted that while just enough and perhaps too much inflammation is bad for a tubercle, a little bit of inflammation either exerts no deleterious effect on it, or may, indeed, be good for it. We see this exquisitely exemplified in studying the influence of tuberculin on *focal* tubercle. All of you are aware that if sufficient tuberculin gets to a focus of tubercle it will cause the latter to react with inflammation. If now the focus is not too large, is not too much of the nature of a diffuse process and is well enough invested to begin with, and if the inflammation is not too intense, we may observe (at

F. P. Mall

BORN SEPTEMBER 28, 1862. DIED NOVEMBER 17, 1917

least, experimentally) the most amazing results to follow the focal reaction, that is, inflammation. In a short time such a focus that may have persisted for weeks and months may disappear like snow before the summer sun, while non-reacted, non-inflamed foci in control animals go on to necrosis and dissemination. But too violent an inflammation in too acute a patch of tubercle can cause irreparable damage from the tissue death and spread of the process that it can bring about.

In the tobacco smoke inhaler we have a comparatively mild irritation, repeated often over a long period. What results is likely to be a chronic inflammation of a low grade. Everything else being equal, its net effects on tubercle that is otherwise being well taken care of should be mildly "stimulating" and tending to repair; not violently upsetting, as might occur from a lobar pneumonia in the area surrounding the tubercle. We should expect, therefore, that a number of divergent and perhaps opposing factors would balance one another, and that, as compared with one thousand non-smokers, a thousand smokers would reach equilibrium.

What I have said applies only to the local irritating effect of tobacco smoke. This effect is to be kept altogether dissociated from any discussion of the constitutional effects of tobacco. Constitutional effects, such as the influence of tobacco on digestion, on the nervous system, on the vascular system, on the psyche, undoubtedly come into play and would have to be reckoned with in any broader discussion of the influence of the use of tobacco on the development of tuberculosis in general.

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MEMORIAL SERVICES IN HONOR OF FRANKLIN PAINE MALL, PROFESSOR OF ANATOMY, JOHNS HOPKINS UNIVERSITY, 1893 TO 1917

A memorial meeting in honor of Dr. Mall was held on Sunday, February 3, 1918, at 4 p. m., in the hall of the Civil Engineering Building at Homewood. Addresses were made by President Frank Johnson Goodnow, of the University; President Robert S. Woodward, of the Carnegie Institution; Dr. William H. Welch, director of the School of Hygiene and Public Health of the University; Dr. Lewellys Franklin Barker, professor of Clinical Medicine in the University; Dr. Simon Flexner, director of the Rockefeller Institute and Dr. Florence Rena Sabin, professor of Histology in the University.

President Frank Johnson Goodnow.—We are assembled here to-day to honor the memory of our lamented colleague and friend, Dr. Mall. Dr. Mall had been up to the time of his death continuously and uninterruptedly associated with the medical school from the time of its opening. He was one of the group who a quarter of a century ago inaugurated a new venture in medical instruction in this country. The purposes which were then outlined, the ideas which were then entertained, the methods which were then adopted had subsequently a widespread influence throughout the land. It is somewhat difficult for us, separated as we are by so long a period from the original time of their formulation and accustomed as we are to the changes which they caused, to appreciate how novel and how important was the work then undertaken.

For the success attendant upon the medical school, Dr. Mall was in no small measure responsible. A brilliant and tireless investigator, he made invaluable contributions to the science to which he devoted himself and won prestige for the institution with which he was connected. A wise and sane counselor, he exercised a potent and salutary influence over the policy of the medical faculty. A kindly and courteous gentleman, he greatly endeared himself to his colleagues and associates.

Passing away in the prime of life and at the height of his powers he leaves in the world of science a gap which it will be difficult to fill, and among his friends a sense of loss which it is impossible to overcome.

We have, however, the satisfaction of knowing that the university, of which he was a member, is better and finer for what he was and did. His life and work will long continue to be an inspiration to the colleagues he has left behind and to the students whom he taught.

President R. S. Woodward, Carnegie Institution, Washington, D. C.—My acquaintance with Professor Franklin Paine Mall began about 20 years ago. We had met casually at that national center of biological interest, Woods Hole, and elsewhere, at frequent intervals during the decade and a half which preceded the more intimate association which began in 1912 and continued with increasing intimacy and attraction until the time of his death. During the year 1912, and especially near the end thereof, a number of conferences were held with him looking to the establishment on a permanent basis, under the auspices of the Carnegie Institution of Washington, of the researches in embryology to which he had long given attention. The conferences referred to and the more intimate relations which followed in the succeeding years brought about a degree of contact and sympathy which enabled us to understand one another to a degree rarely attainable. This experience has been especially interesting and instructive to me, and there appear to be the best of reasons to assume that it was similarly interesting and instructive to him. From its inception Professor Mall applied his unusual capacity for interpretation of the minds of men to me, and he appeared to be equally conscious of the fact that I endeavored also to make a special study of him and his char-

acteristics. I am not aware that he made any record of his observations upon me; there was no occasion for him to do so; but the untimely termination of his terrestrial career and the present memorial occasion seem to render it permissible to make acknowledgment of, and to record here, the impressions he produced upon me.

Since my association with Professor Mall had much to do with purely business affairs, in the development of his department of research, it is not improper to speak of his business abilities, although the world at large would probably not credit him with the possession of noteworthy capacity for fiscal affairs. There is, indeed, still, even in the twentieth century, a widely spread belief that men who are devoted to the pursuit of science, or to activities whose results are not measured in dollars and cents, are conspicuously lacking in business capacity. But this is a fallacy which will disappear under a closer study of the fundamentals essential in the effective conduct of affairs. It is commonly held, particularly in government circles, that those only possess executive ability who are trying to exercise it. Thus it is possible for one who has few qualifications essential to effective conduct of affairs to derive credit for remarkable capacity in such work, especially if he be able to depend upon subordinates to prevent him from going wrong. On the other hand, it is often said that executive ability consists in doing well what ought not to be done. But it would be wiser to say that executive ability consists in doing well and without ostentation anything that is worth doing. In this better sense of the phrase Professor Mall excelled. He possessed uncommonly clear vision. He held adequately considered theories of procedure, and he entertained a rational perspective of the relative importance of the factors involved in any case. He possessed all the elements, therefore, of superior capacity for the ordinary affairs of life, although he was never called upon to concentrate his attention exclusively on them.

His life was given rather to research, and his theory and practice therein are deservedly worthy of special attention. He held very distinct views on this subject. He understood very clearly that progress, resulting from research, does not consist simply in innovation, much less in eccentricity. He understood, likewise, that progress does not consist in the mere accumulation of facts in accordance with well-known methods. He had no fear of breaking with precedent. His criticisms were sometimes mistaken for iconoclasm; but while they were often destructive, they were also, in general, highly constructive. He was exceedingly fertile in suggesting better ways of doing things even in matters which lay outside his special interests. Whatever entered his mind was visualized in a variety of aspects. He was surprisingly quick in separating the essentials from the unessentials of any question presented to him.

Of his work in science, I am not qualified to speak except in general terms. He was a specialist in certain branches of biology, and in these he developed processes peculiarly his own. But in their general aspects his methods are the well known methods of science, and one does not need to know much of his technique to discover the reasons for his remarkable capacity for productive work. His sincerity, his industry, and his comprehensive knowledge of his work carried with them conviction and confidence. He entertained always a clearly definite plan for any piece of work, having set items in his program for every step from the initial observations, investigations or data, to the final publication of the results and the distribution of them to experts who might be expected to appreciate and hence to make effective use of them. He understood uncommonly well the value of system; but he never permitted the mere machinery of research to absorb his attention or to deflect him from his principal objects. He made extensive use, for example, of card catalogues and bibliographies but always as means to rather than as ends in his investigations.

Professor Mall possessed certain notable characteristics which were manifested in striking fashion often in conferences with him concerning subjects of special mutual interest. He was a man of few words, he was never prolix in argument, and he knew well when a conference was finished. He was able always to concentrate attention on the salient features of a subject under discussion. He was extremely reasonable with respect to matters of controversy and this made it a source of pleasure to confer with him even when differences not easily dissipated arose; for his manifest desire to have the adjustment of every question depend on its merits was always an assurance that the right conclusion would be ultimately reached.

Summarily characterized, Professor Mall was an ideally typical man of science. He tried to visualize the universe as it is; or, in more common parlance, he looked at, and sought always to see, things as they are. His perception of reality and his conformity to it were noteworthy in all his activities. He was able to see much more clearly than most of us that limitations exist on every hand. Men of science, generally, and mathematicians even, are not infrequently found to entertain an inadequate respect for the rules of elementary arithmetic; but this is a defect of the human race rather than of any class of men, as is well demonstrated by the fact that professional financiers show least respect for those rules. But in an age when many good men have lost their heads, temporarily, at least, in respect to the possibilities of the ways and means available for promoting research and discovery, the equilibrium of Professor Mall remained undisturbed. His foresight was singularly free from the fogs and the illusions which often diminish the efficiency of enthusiastic investigators. He knew well how to count the immediate costs as well as to estimate the ultimate consequences of the researches to which he was devoted.

Quite naturally and gracefully the mental qualities already alluded to were supplemented by correspondingly high moral qualities. The two kinds of qualities were, indeed, inseparable in him. They were neither stored in separate compartments nor restricted in use to separate days or occasions; the entire man was always visible and available in his presence. Where he stood, or what he thought with respect to any question to

which he gave attention was never a matter of doubt. He faced his colleagues with the same frankness and the same truthfulness with which he approached the problems presented by his favorite science. It is in this rare combination of mental and moral traits that we find the foundations at once for his signal success as an investigator and for the affectionate and abiding regard he won from all those who had the good fortune to share in his more intimate friendships.

Dr. William H. Welch (Abstract).[1]—Dr. Welch outlined briefly Dr. Mall's medical training and the steps which led him to the laboratories of His and Ludwig in Leipzig, where he and Dr. Welch first met in the winter of 1884-85. Speaking of the great influence which these two men had upon his scientific development, Dr. Welch said:

Ludwig's was, I believe, the stronger and more personal one; that of His was more in methods and the specialized problems of embryology. I had worked in Ludwig's laboratory 10 years before and he often spoke to me rather freely. I doubt if he ever had a student to whom he was more attached, or who had made a more profound impression upon him that Mall. He more than once spoke to me of Mall's remarkable intellectual qualities.

At that time Dr. Welch had already been called to The Johns Hopkins University, and upon his return to America he received a letter from Dr. Mall expressing a desire to come here and work. In consequence he came to Baltimore in 1886 as fellow in pathology.

While in the pathological laboratory he was, as you may imagine, an independent worker; it was a delight to have him there. He assisted in the course in bacteriology, and his methods then had the same originality that has always characterized them. He was interested in connective tissue and discovered that certain varieties of bacteria had the power of digesting certain kinds of connective tissue.

At the end of three years he went with Professor Stanley Hall to Clark University, and later to the University of Chicago. He had made the acquaintance of President Harper while in Leipzig, and the two were close personal friends. It was with some misgivings, therefore, that Dr. Welch, at the request of The Johns Hopkins University, set about to induce Dr. Mall to return to Baltimore at the opening of the medical school in 1893. The plan of the school, however, appealed strongly to Dr. Mall, and although every effort was made to keep him at the University of Chicago, he accepted the new post. Of his work here Dr. Welch said:

Mall belonged to the group made up of those men who came in the early days of the hospital, in 1889, and those who came as workers in the scientific laboratories of the new medical school in 1893. He is the first of that group to be taken away. I think my colleagues will agree that, of all that early group, he was the most productive contributor to science and one of the most stimulating influences. There is no expressing the loss which this school and university, and we, his colleagues, have suffered. He was wise and sound, and had a great insight into the value of things. I know of no one whose powers of mind were more penetrating. He, more than any of us, perhaps, represented two of our educational ideals—freedom in teaching, freedom in learning, freedom of the teacher, freedom of the student. Indeed I may say that President Gilman, having once selected a man whom he considered qualified as the head of a department, left him a pretty free hand. Mall entered into that spirit most thoroughly, and was undoubtedly a very inspiring influence for the better students. That was one of the ideals he stood for. The other was, that the primary qualification of a preceptor should be the capacity to produce or to stimulate production. These two ideals he never lost sight of, and in him they were exemplified to a surprising degree.

He was to all of us a delightful companion, and it was a joy to be with him. He was attractive and had a whimsical way of saying things, but he was very wise. He ranks with Rowland as one of those men who have added lustre to the university by their contributions to science, and who, by their revolutionary influence upon their subjects and their great capacities as teachers, have led others to become teachers. One has only to consider what anatomy stands for in our medical schools to-day, as compared to what it was when Mall began his work, to appreciate what his influence has been upon the science of medicine. His memory is, indeed, one of the most precious possessions, not only for us, his colleagues, friends and admirers, but for all times of this university.

Dr. Lewellys Franklin Barker.—Adequately to present the personality of Franklin Paine Mall, to describe the essential qualities of his character, and to do justice to the distinctive excellences of his intellect, would require the pen of an expert psychographer, the selective ability and the power of artistic composition possessed only by a skillful naturalist of souls. It is to be hoped that, sometime, an experienced practitioner of the art may supply us with the fair and right account that we should like. Those of us—pupils, colleagues, and friends—that are gathered to-day at this memorial meeting can scarcely do more than contribute materials and clues that may later on be an aid to the definitive production that will be proportionate and satisfying.

No one who enjoyed close association with Mall during his 25 years professorship at The Johns Hopkins Medical School could fail to recognize a unique personality, whose significance for medical science and especially for anatomy in this country was outstanding; and those who were admitted to the circle of his friends counted the experience as one of the most rewarding and precious of the privileges of their lives. For some five years it was my good fortune to be his assistant in the anatomical laboratory here, and, seeing him daily in his work, I had manifold opportunity to become impressed with his powers and his activities as investigator, as teacher, and as educational reformer; and, above all, I came to know him as a man and a friend. Concerning his work as an anatomist Professor Sabin is to speak; I shall refer to his anatomical work only in as far as it throws light on the intellect and character of the man.

Mall's greatest professional interest lay in the promotion of original research in anatomy and especially in human embryology. His appetite was whetted for the pleasures of the intellect. He enjoyed accumulating facts but he longed still more for that most exalted of intellectual pleasures—the discovery of truth. He had an inexhaustible enthusiasm for the

[1] Owing to the continued absence of Dr. Welch in connection with his work in the office of the surgeon-general of the army, it has not been possible to give his address in full.

study of form and particularly for inquiries into the genesis of form. He delighted in finding (and fixing in enlarged reproductions that are permanent records) the several stages through which the body, or a part of the body, passes from its first formation in the embryo onward toward complete development. In his opinion, not much progress in human anatomy can now be expected from mere dissections of the adult human body; advances in our knowledge of human structure can come only by way of microscopic and chemical studies of the parts or by investigations into the genesis of the organs and tissues of man and animals. An institute that attempts fairly to represent the subject of anatomy must, of course, be prepared to teach and to study the mature body of the highest animal form, but it must also, he thought, concern itself largely with the origin and development of the individual being (ontogeny) and with the racial evolution of the type (phylogeny). Though his own interests lay more in embryological than in comparative anatomical inquiry, he had a deep sympathy with both modes of attack and was ever ready to encourage researches in either direction. His attention was early drawn to pathological human embryos and throughout his life he collected these as well as normal forms and subjected them to intensive study by the newer methods. Though predominantly a student of form, he was by no means insensible to the delights and the rewards of the study of functions; indeed a number of his researches were directed toward the solution of what might be designated physiological-anatomical problems, such as the determination of the functional-structural units in the liver and of the vascular supply of the several viscera. The influence of the teachers that inspired him—Welch in pathology, Ludwig in physiology and histology, and His in embryology and histogenesis—was evident in the directions that his work took, but his period of tutelage was brief, his problems were his own, and he will always be distinguished as one of the independent thinkers and investigators of our time.

His method of teaching was unusual. He rarely, if ever, lectured. Not that he thought the lecture of no didactic value; on the contrary, he was a firm believer in its stimulating effect when properly prepared, illustrated and delivered. But he felt that he himself could teach better in other ways, and he relegated the lectures to other members of his department. He was, however, a master of what is called "elbow-teaching," and no student who has ever been at his elbow will ever forget the character of this relationship—his trenchant comments, his startlings of the intellect and emotions, his humorous and sometimes satirical thrusts, and, above all, his earnest and sincere desire to make the neophyte an independent worker. New students often failed to understand him. Accustomed in the college of liberal arts to lucid exposition, to measured tasks of memory, to recitations on text-book reading, and to the performance of laboratory work so carefully planned and described as to leave but little room for personal initiative or for independent thought, many of the freshmen in the medical school felt "lost" when they were told by the professor in his white gown to begin the dissection of a part, using atlas and text-book as guides, without any special instruction as to where or how to begin, without description of what was to be observed, and with no intimations that definite amounts of work should be performed in given spaces of time. Of course, they floundered, and often they bitterly complained. The method was drastic, and some, I fear, never understood its purpose. For most students with good natural endowment, however, the compulsion to realization of the fact that on entrance to the medical school the period of spoonfed education was over and that the time for acquiring the power to work more independently had arrived, though abrupt and perhaps painful, was most salutary, and I have heard many a student admit that he owed to Mall's method his intellectual awakening and his first arousal of desire to become an independent scientific worker. Mall's contempt for slovenly or dishonest work, his admiration of a rigidly perfected technique, his encouragement of objectivity in study, his insistence upon familiarity with the bibliographic sources, his emphasis upon the duty and pleasure of extending, rather than upon merely acquiring, knowledge, his impatience with inaccuracy and with stupidity, his unswerving loyalty to the highest ideals of natural science—all were qualities that made him a working companion of inestimable value to the young men and women who entered The Johns Hopkins Medical School. His influence upon the rank and file of the students, large and beneficial as it was, was even exceeded, however, by the effect he had upon the small group of more original minds in each class and upon the members of his staff. Mall had a nose for the potential scientific investigator. With almost unerring accuracy he would scent out young talent and give it special encouragement and opportunities. Not all buds, it is true, opened in that atmosphere—a number have found conditions more favorable to the unfolding of their special talents in other departments later in the course—but it is interesting in looking over the scientific publications of graduates of our medical school to note how many of their authors began to evince an interest in original inquiry while in the anatomical laboratory. It was largely owing to Mall's early capture of promising young minds that so many have found a career in anatomy interesting and satisfying, and that a large number of the chairs of anatomy in American medical schools are now filled by his pupils. A still larger number who were led by him to undertake original inquiry have continued to be scientifically productive in other fields of medical science, preclinical and clinical. It was a principle with Mall that any department in a university should teach its subject for its own sake, without too much concern for its application to the work of branches to be pursued later in the student's course. He maintained that it was not the business of the department of anatomy to teach the so-called surgical and medical applied anatomy, for these subjects properly belong, he asserted, to the departments of surgery and medicine. From this position he could not be budged, either by the imprecations of clinicians or the threats of State Board Examiners. By his own special methods of teaching, however, and with the aid of a carefully selected and well-organized teaching staff, he fulfilled the

function of a university teacher, for he saw to it, first, that undergraduates secured a knowledge of the main facts and principles of his science and some acquaintance with its practical-technical methods of investigation; and, secondly, that numerous workers were induced to pursue anatomy as a career, devoting the rest of their lives and energies to the teaching of the subject and to original inquiry in some one of its divisions.

Though the character and intellect of the man are well revealed by his activities as investigator and as teacher, it would be remiss not to speak of his ability as organizer, and of his wisdom as counsellor and educational reformer. Mall appreciated more perhaps than most directors of scientific institutes the importance of the best material equipment for his laboratories, and made rigid rules to provide for its care and to prevent its deterioration. He trained technical assistants to relieve the scientific staff of much routine work. He believed that every laboratory director should be a good housekeeper, and the scrupulous cleanliness and perfect order of his institute, marvelled at by all who had grown up under an older anatomical regime, reflected his opinion that the character of the surroundings in which people work exerts a moral effect upon their conduct. Mall's organization of the Anatomical Laboratory of the medical school and later of the Embryological Institute of the Carnegie Institution was based upon a differentiation of function and a corresponding division of labor among the members of a staff. He knew how to delegate large responsibilities to subordinates, how to correlate the several activities of his department and how to maintain the oversight that is necessary to ensure the satisfactory progress of work. Indeed, he made his own the three watchwords of every successful executive, "Organize, Depute, Supervise."

As a counsellor, Mall's advice was sought not only by those interested in anatomy but, and especially, by the leaders in this country of reforms in medical education. University presidents, heads of science departments, members of the directing boards of scientific institutes, and professional investigators of the evils of existing educational systems, conferred with him and were profoundly influenced by his opinion. In a number of articles that have been published since 1890 upon the improvement of the conditions in our medical schools and hospitals, the "insider" will have no difficulty in recognizing the tricklings from a well-known stream. He favored the foundation of whole-time clinical chairs in our medical schools and the writers who first urged this reform owed their seed-thoughts to stimulating discussions with him. In faculty meetings, and in large groups generally, Mall was retiring and for the most part silent. He was at his best tête-à-tête, for under four eyes, or in small groups, his taciturnity disappeared, and his speech to the sympathetic listener was free and always inspiring. His conversation was peculiarly stimulating to his friends on account of a certain cryptic character that depended on the frequent elision of associative links. His own mind worked so rapidly that it appeared to make leaps rather than to flow, and the interlocutor who was not agile enough to leap with him, or to intercalate for himself the materials necessary for continuity, would sometimes be at a loss to understand him. More than one man has been heard to say that he "could not make head nor tail of what Mall was saying." But to him who could and would follow, how rich was the reward! Mall's example as an organizer, his wisdom as a counsellor, and his zeal as an educational reformer, have given the progressive movement in American science an impetus that will continue long after his death.

A man absorbed in scientific pursuits does not always take time for the enjoyment of home and friends, or for the satisfaction of the æsthetic desires. But Mall was singularly happy in his home life and no one ever had stauncher friends or was more loyal in friendship than he. Married in 1895, he found in his wife one who could sympathize fully with his work, who could share his ideals, who, with him, could disdain mere externals, and who felt it no sacrifice to give up many material and social pleasures when they conflicted with the interests of the higher intellectual life. To their home, personal friends were always welcome, and on Sundays and holidays members of the laboratory staff were frequently entertained there. Mall's personal solicitude for the welfare of members of his staff was touching. His suffering was acute when they were in trouble, and when successes came to them he was elated. He had no desire for, or satisfaction in, promiscuity of social relationships, but wherever he was—at Clark University, at the University of Chicago, or in Baltimore—he drew to himself a small but congenial group of intimates, and to them he gave himself freely. Those thus advantaged were impressed with the fusion of sound sense with earnest enthusiasm that was characteristic of him. A little tinged with pessimism, he was, in reality, a meliorist, knowing that there is much to do (that can be done) to better man's estate. He had strong faith in the beneficent power of truth and of work. He believed in freedom of thought and he practiced freedom of speech. He was a striking example of a strong and a liberal spirit. Memory of him will continue to move the souls and to keep warm the hearts of those who knew and loved him.

Dr. Simon Flexner.—The death of Doctor Mall is so recent and my grief for his loss so fresh that I find myself reflecting on the fruitful and delightful memories of our past association instead of writing out my impressions of his unusual personality.

Doctor Mall returned to Johns Hopkins in the late summer of 1893, just before the medical school opened its doors to the first class of students in the autumn. It was then that we met. I recall vividly my excitement and nervousness when the rumor was circulated about the old pathological building that Mall had arrived. His name had been a tradition among the small group in the pathological department. A few years earlier, before the hospital had been opened to patients, he had come to the laboratory and, as fellow in pathology, had performed a miracle of interesting and important studies on the connective tissue foundations of the organs. Fellows in

pathology there had been since his time, but no one whose memory was glorified as Mall's had been. We had so often heard him and his work spoken of by Doctor Welch, Doctor Halsted, and others, including the indispensable Schultz, who was for many years presiding genius over the technical and janitorial services of the laboratories and whose commendation carried with us such great weight, that I pictured Mall as quite different from what in actual life he proved to be.

One's fancy—my fancy surely was so—when young is apt to produce its own pictures. In my fanciful portrait of Mall I represented him as large, absorbed, and rather austere. Never was a fancy more completely and happily shattered. I can just remember our meeting; those who knew Mall well will never forget how engagingly he smiled. It was with one of the best of his smiles that he greeted me.

That event was the auspicious beginning of a warm friendship which never wavered until his death. During the first period of half a dozen years we were in almost daily contact. Later, and after 1900, when I left the medical school to enter the University of Pennsylvania, our meetings were at first not infrequent. I shall never cease to regret the increasing intervals between them which followed my removal to the Rockefeller Institute in New York. Increasing responsibilities and broadening duties play sad havoc with one's life, and I feel that I suffered a grievous and now irremediable loss in permitting those circumstances to cut me off to the extent it seemed inevitable they should from association with Mall. To a certain extent, letters took the place of personal contact. Thus I kept more or less in touch with the workings of his restless and constructive mind.

It probably will strike few except his very intimate friends that Mall was by temperament a reformer. He was an uncompromising democrat and hence entertained the firmest belief in liberty in its true and proper sense. Out of this intensity of conviction arose the views expressed in conversation more frequently but not more forcibly than in his addresses, on full opportunity and freedom in university education, both in its pregraduate and postgraduate aspects. His comprehending and incisive mind was the first, I believe, to appreciate and afterwards to propound that the best of medical educational institutions were half-hearted affairs. The part of the institution which a quarter of a century earlier had been the weakest—the laboratory branches namely—had been immeasurably strengthened in that short period, during which the previously stronger part—namely the clinical branches—had progressed relatively little. The balance could be struck and must be, even though in the process the old system were, if need be, completely shattered, as much shattered indeed as had been the earlier hybrid combined laboratory and clinical chairs. Out of this conception which Mall propounded, I am almost inclined to say preached to us persistently, arose the present movement ever gaining force and strength until it has now become almost irresistible, in favor of full time clinical professorships.

It is very interesting to consider just here the extent to which he used others, converts or disciples as they may be called, to diffuse more broadly his reforming ideas. One would search Mall's miscellaneous papers, of which, indeed, there are notably few, in vain for an exhaustive presentation of the case for the full time clinical plan. The wide dissemination of the idea by the printed page was left to others, while he maintained the high level of conviction in those coming under his immediate influence by an irresistible fund of logical exposition.

In his delightful essay on his master, Wilhelm His, Mall reveals his attitude toward higher education in its various complex aspects. I wonder how many returned foreign students have kept up an intimate correspondence with a revered teacher extending over a long period of time, like that disclosed by Mall in this essay. The extracts from his letters there published show how well the older man comprehended the younger, as the spirit and substance of the essay show how the younger man admired and appreciated the older. There is no doubt that His perceived in Mall rare personal and mental qualities, as he confides to him not only the subjects and trend of work, but his larger aspiration in the wide domain of anatomical research. In the light of the relation there revealed one can surmise the satisfaction and joy with which His, had he lived, would have welcomed the establishment of the Institute of Embryology with Mall as the first director.

In my task of presenting a fragment of the personality of Mall as apparent to his intimate friends and associates, I find myself embarrassed by the many memories that crowd my mind. It is not easy to select episodes. I love, myself, to think of the period during which he lived, as did the medical officers, in The Johns Hopkins Hospital, for then we were almost constantly together. The small, older group of men—older, that is, than the internes—saw much of one another. Mall, Frank Smith, Thayer, Barker, and I met always at dinner, frequently at breakfast and luncheon at the small table at the head of the room. There was lively conversation and much variety of theme; and not a little good cheer. A small photographic print still exists which pictures the group; it is chiefly notable for the good likeness of Mall which it presents, showing him as it does in one of his happiest moods.

Mall returned to Baltimore as the first professor of anatomy of the new medical school. The physical conditions surrounding the launching of the medical school were so simple as to be almost austere. Aside from the hospital—a model of completeness at the time—the plan for housing the new departments of the school we should now regard as meager in the extreme. I sometimes think that it may be well to recall from time to time the simple beginnings out of which the great institution of The Johns Hopkins Medical School arose. The only additions made to the hospital buildings, to accommodate the departments of anatomy and physiological chemistry and pharmacology, were two stories added to the original small pathological building erected as a mortuary for the hospital and already housing the entire pathological department. It was in the upper, or fourth story of that enlarged building that the complex department of anatomy took origin.

Some one else, who traces the growth of anatomy at the medical school, can tell better than I can how Mall adapted the limited space and facilities at his command to the teaching of anatomy, histology, and embryology, and to the conduct of research. There was no actual break in the continuity of his own investigations, and very soon after the medical classes were taken in he began to produce the new work which in a steady and increasing stream has come out of the anatomical department.

There were not a few obstacles to be overcome in getting the student's work properly started. I recall the shifts he was obliged to make to bridge over the gaps in dissecting until human cadavers became available. This period was for Mall, in many ways, an anxious one. But it was not long before this particular obstacle was overcome, and because of the improvements which he introduced in the preservation of human cadavers, his laboratory soon became the custodian of all the anatomical material employed for dissection and surgical instruction throughout the city.

The kind of teaching which Mall gave to his students has been described; there was no lecturing in his curriculum. He had almost a horror of lectures in anatomy; the idea collided with his fundamental conception of how so practical a subject is to be acquired. In his views there was one road only to that goal. The student must teach himself in order to learn. Hence there were provided the objects to be dissected, text-books, atlases, models, and time, with a sufficiency but no excess of instructors or guides. He saw no virtue in exhibiting and describing a predissected part, provided the students were given opportunity to dissect for themselves. That this principle is sound no one will, I think, now deny. That its operation has produced a remarkably large number of superior, independent, and broad anatomists, the history of his department amply shows.

But a confusion of method and man is often made with disastrous consequences. It is easy to imagine this mode of teaching anatomy adopted widely without yielding the results which Mall obtained. To put the method into effect would doubtless represent a great advance over the old system, but without a strong, able teacher and guide, such as Mall was, the phenomenal results which he achieved would not be attained. In other words, he was a sound innovator because he was a strong man. He was a successful leader in anatomy because he was learned and original. He has left a rich heritage to science through his own labors and those of his pupils, because to all his other qualities he added the rare ones of wisdom, kindness, and generosity.

Our proximity in the pathological building brought us into frequent association. In the early days of the medical school, Mall often attended the autopsies, many of which I performed. His active interest in the pathological phenomena continued throughout his life, in part possibly as the result of the year spent as fellow in pathology under Doctor Welch. But in fact he did not dissociate, as is often erroneously done, facts of pathology from those of anatomy. Being naturally inquisitive in regard to the relation of cause and effect in respect to the unit forms of organs, he was also prone to inquire into the effects of causes in their nature pathological.

At about the period when Mall was studying the lobular unit of the liver I was induced to attempt the application of some of the methods he worked out to cirrhosis of that organ—a mere illustration of the way in which two related departments through him were made to react on each other.

I imagine that few who knew Mall even quite well realize with what intensity of absorption and application he would work at a problem once he had gripped it, as one might say. In temperament he was naturally reflective. Hence there occurred periods during which he appeared to be doing little in his laboratory. At such times he would become possessed with the impulse to roam about the building or out into the city or into the adjacent country. It was remarkable that when under the influence of those moods he did not seek solitude so much as another form of activity. I was not infrequently taken away by him for a stroll through East Baltimore, and on these expeditions I acquired quite a knowledge of that part of the city. They were in many ways extremely interesting occasions, for during them he often talked his best and sketched advanced ideas on educational and other reforms, as well as on problems of research. I think Mall never dreamt idly. He was possessed of a romantic imagination, but it was both controlled and constructive. To not a few who did not understand him well his ideas sometimes sounded extreme, but they invariably rested on real foundations, as is now evident since so many of them have been carried into practical affairs.

At other times he worked out problems in his laboratory with consuming intensity. It would seem as if while under what I have called the spell of his reflective mood, a problem would formulate itself more definitely, or some barring obstacle give way to a revealed point of view. However that may be, my notion was that the periods of reflection were signs that he would attack a new or solve an old problem; and I always looked for new ideas and accomplishments when the mood changed.

If I have at all succeeded in revealing Doctor Mall as he appeared to me, then I have presented to you a complex personality. The remarkable thing is the way in which all the pronounced qualities that characterized him were fused into a simple, harmonious, kind and lovable individuality. I have referred already to Mall's democratic spirit. He was an intense lover and active exponent of liberty. His belief and confidence in freedom extended far beyond the confines of the university and laboratory, and into the world of politics and government. Freedom within the university he held as the first condition of the successful struggle of the forces of light over superstition and darkness. Within the walls of his laboratory the fullest liberty prevailed. Once outside the realm of the prescribed task for training, each man followed the bent of his own talents and tastes. However, his principles as well as his practice sharply differentiated between liberty and license; hence the rise under him of a group of strong, independent, but sound teachers and investigators. Mall would probably have combated the suggestion that he produced a

school of anatomists, using the term in its usual significance. He would probably have insisted that he merely continued in America the system which he pursued or saw in force in Switzerland and Germany. But I believe rather that he made such definite contributions to the higher education and training of anatomists, and produced in, alas! a few brief years so large a number of varied and capable teachers and investigators, as to mark a new era in the history of higher educational endeavor.

I said that his deep convictions on freedom carried him into the wider domain of social liberty. Mall never propagandized on this subject. Nevertheless, he felt intensely about it. It is noteworthy that with all the admiration for the freedom of migration from university to university and the wide election of subjects and ideas in the German university, to the social and political conditions of that country he was antipathetic. To so strong a "democrat," to use that term in its wider and better significance, a studied paternalism and imperialistic tendency were deeply unsympathetic.

Mall's sincerity, self-effacement, and never failing consideration were at the root of his noble qualities and made companionship with him a rare privilege. I have already spoken of my own good fortune in possessing in some degree his intimate friendship. It is a rare possession, indeed, and one to be cherished. But I owe him also an educational impress, none the less valuable because of its subtle nature. I am of the opinion that his pupils were influenced by this unusual quality which because of its elusiveness seems an emanation—so little was it given off or received with immediate conscious perception.

Mall was absorbed in ideas. They formed the substance of his serious talk, but he was by no means a stranger to the lighter side of human relations, for he possessed a gentle and engaging humor which might even, when provoked, become a little biting. It took time and skill to penetrate an outer film of reserve which arose from innate modesty and shyness, but once beneath that protective covering, one readily discovered in him a simple, idealistic, and gifted person of many sides, possessed of an almost miraculous power to stimulate students to put forth their best efforts. His memory and example will long survive in the achievements of his students and associates, in the broad ideas which he disseminated, and in the admiration and affection which he inspired.

Dr. Florence Rena Sabin.—To those who are familiar with the history of medicine in this country it is a matter of common knowledge that at the time Dr. Mall began his career, 30 years ago, anatomy in America had no scientific standing, a mere tool of surgery, with but a single method, that of dissection. He left it where it must be, and always has been in any community where medicine is progressive—one of its great sciences. He has left it richly endowed with technical methods, a science so truly fundamental that the workers in every other branch of medicine are constantly and increasingly returning to it, both for methods and results. The vision of this change must have been his while he was yet a student for he wrote in one of his letters: "My aim is to make scientific medicine a life work. If opportunities present I will. This has been my plan ever since I left America and not until of late (since having received encouragement) have I expressed myself. I shall no doubt meet many stumbling blocks, but they are anticipated."

Sweeping aside the traditions of the dissecting room, he first created conditions under which this change could develop, and then devoted himself to scientific achievement, and to the type of teaching in which he was profoundly interested. It was one of his oft repeated maxims, that the best, and perhaps the only great way to teach, is by example. With the ideal of scientific work as his goal he has left us an example so rich in ideas, so varied in technical methods and so representative of the range of anatomy and embryology, that a study of his work is both an inspiration and an education.

His very first undertaking in the field of research serves well to illustrate his independence of thought which to those who knew him was one of his most striking characteristics. During the winter of 1885 he began his scientific work under His at Leipzig, who gave to him the study of the gill-arches in the chick. Four years prior to that time His had studied the same region in a human embryo. He noted that the gill-arches do not break through into the pharynx, but that a depression of the ectoderm develops over the region of the third and fourth arches, and concluded that the thymus must arise from the ectoderm of this depression. Dr. Mall evidently made his study independently, cut his own series, made reconstructions and came to the conclusion, now generally accepted, that the thymus arises, not from ectoderm, but from the endoderm lining the pharynx. At the end of the winter's work he presented his results to His in the form of a finished manuscript in English. His could not, however, accept this conclusion so directly opposed to his own view and asked his pupil to restudy the subject. This he did the following winter while in Ludwig's laboratory, translating his manuscript into German. The work was given to His a second time and accepted for publication, just as Dr. Mall was leaving for Baltimore. In the next number of the journal of which His was editor, there appeared a second communication from the latter, strengthening his own point of view, but announcing that a different opinion would be published by one of his pupils in the next number. When Dr. Mall's article appeared it was with a damaging footnote by His, to the effect that the independent character of the results was obvious. During his early months in Baltimore, Dr. Mall established his point in a mammalian embryo, and two years later His restudied the region in a human embryo and found that Dr. Mall's conclusions were correct. He gave due acknowledgment in an open letter to Dr. Mall published in the same journal in which he states frankly, "Sie haben gegen mich Recht."[1] This letter cemented a life-long friendship, as can readily be seen from the correspondence accompanying Dr. Mall's article, "An estimate of the work of His."

[1] His, W.: Schlundspalten und Thymusanlage. Aus einem Briefe von W. His an F. Mall in Baltimore. Arch. f. Anat. u. Phys., Anat. Abth., 1889.

During the winter of 1885, His suggested that Dr. Mall work under the great physiologist, Ludwig. As Ludwig's laboratory was always full, the opportunity was slow in coming; indeed, as Dr. Mall wrote home, he was leaving Leipzig with no hope; his trunk was even on the way to the station when the letter came that the opportunity he so much desired was his. So great was the influence of Ludwig over his mind, character and future work that it is impossible to overestimate it. He himself summed it up in these words, "To that master I owe much—all." Ludwig assigned him the study of the villus of the intestine. As he stated in one of his letters almost his first impression was that here was a subject which had occupied the minds of the greatest anatomists of the past century. Repeatedly throughout Dr. Mall's writings there is to be found that expression of regard for the work of great minds. Widely read in his own subject, it was of the works which have lived and will live that he made a profound study.

In Ludwig's laboratory Dr. Mall learned the methods of injecting blood-vessels and lymphatics, and his studies of the vascular system of the intestine and stomach are familiar to every student of medicine. Under the influence of Ludwig, his work was characterized by a very strong physiological bent. Indeed, it may be said that his work was physiology in the hands of one with an intense interest in structure. In the work on the intestine, and more clearly still in that on the stomach, he was absorbed in the mechanism of all the parts of the organ.

In some of the foreign universities it was the custom for a new incumbent of a chair to deliver an address giving, as it were, a "prophecy" or a "program" of his future work. Such a program was the famous address of His on accepting a chair in the Swiss University of Basel. In some such way the article of Mall on the stomach, published in the first volume of The Johns Hopkins Hospital Reports, gave his program of the way in which he proposed to study anatomy. This paper lays a foundation for what may be called *physiological anatomy* and in it can be traced the beginnings of many of Dr. Mall's ideas. He studied the stomach from every aspect and with a wide range of methods. There were experiments in digestion bringing evidence to support the view that the acid is secreted only in the region of the fundus; here is the beginning of his brilliant studies on connective tissue, in which he became interested through noting the arrangement of the fibers of the submucosa. Here also are observations on smooth muscle which led to the study of the types of contraction-waves in the intestine, and later to experiments on the reversal of these waves. In his paper on the stomach is this brief note: "Recently I have found that irritation of the splanchnic nerve causes contraction of the mesenteric vein." He probably first made this observation in Ludwig's laboratory, and subsequently proved that the portal vein is supplied with vaso-motor nerves, one of the valuable discoveries in physiology.

The most important idea of his early work from the standpoint of anatomy, was that of structural units, which Dr. Mall conceived from the study of the villus. He noted that the villus was the unit of function of the intestine, and this theory of structural units can be followed through a long series of investigations, in part by himself and in part by his pupils. In fact almost every organ of the body has now been studied from this point of view, and almost every organ except the nervous system can be simplified by this conception. The theory reaches its best expression in Dr. Mall's own articles on the liver and spleen, in which he states that organs are made up of ultimate histological units represented in the vascular system by the capillary bed which intervenes between a terminal artery and its corresponding vein. At this point the two cease to accompany each other and are separated by the maximal distance, that is the length of the capillaries. Thus the length of the capillary determines the size of the unit. These ultimate histological units are grouped together into lobules which vary considerably in the different organs of the body. They are not only of great structural significance, since an organ is to be considered as a multiplication of them, but are also of significance to physiology, since such units are equal in function. For example, a unit of a gland gives a unit of secretion. This equality in size and function comes from the laws of growth of an organ; when a unit increases in size, so that the length of its capillaries increases beyond the norm, a new artery develops, the single unit splitting into two. Thus, from the general theory of structural units, Dr. Mall was led into one of the aspects of the problem of growth; namely, how a small organ becomes a large one. This problem he often discussed in the laboratory. In his article on the liver he gives the clearest expression of it. There he develops the theory of Teile and Sabourin that the portal unit, not the hepatic lobule, is the real unit of structure and function, since the portal units are equal in size and are also the centers of growth in the liver. During growth these units are constantly fractured and destroyed as new units develop, and it is this interstitial growth in organs which makes the subject so difficult to follow.

In his study on the spleen Dr. Mall brings out best the relation of all the tissues of an organ to its function. Thus the spleen is an organ based upon the vascular system; its histological units are grouped into lobules which are outlined by dense bands of connective tissue. The arteries in these lobules end in swellings—the ampulla of Thoma—where the endothelium changes from the typical complete lining of a blood-vessel and becomes a reticulum with open meshes. This change in the endothelium, demonstrated histologically by Mollier in 1911, had been fully described by Dr. Mall 11 years earlier. Through these openings in the ampullæ both the blood-plasma and the corpuscles pass freely into the pulp and thence back into the rich plexes of veins which fill the lobule through corresponding holes in their walls. By experiments Dr. Mall showed that the emptying of the pulp-spaces into this plexus of sinusoidal veins is accomplished by means of the contraction of the bands of smooth muscle in the trabeculæ. As these bands contract, the trabeculæ of reticulum upon which they run tend to pull open the interlobular veins, while at the same time they compress the arteries. Thus the splenic pulp, one of the most difficult enigmas in histology, is seen to serve as the capillary bed of the spleen. This study of structural units

grew out of the work in Ludwig's laboratory, and may be considered as the foundation for a new phase of anatomy, a step beyond morphology, *i. e.*, the study of the adaptation of the minute structure of organs to their function.

More than any other anatomist, Dr. Mall has also enriched our knowledge of the fibers of the connective tissue. He analyzed the differences between elastic fibers, white fibers and a modification of the latter—the reticulum, which forms the framework of organs. In this study he used the methods of bacteriology and of chemistry, adapting them to his needs and producing the most beautiful specimens of reticulum to be found in anatomical literature. This study he illuminated by showing that the framework of organs is not an inert structure, but is adapted to the function of each organ. His account of the origin of the fibers of connective tissue from cells, though recently called into question, will, I believe, hold.

One of his valuable contributions is the study of the structure of the heart. He grasped the significance of the work of Krehl, which he said bore the stamp of Ludwig. Krehl demonstrated that when a heart is macerated in a weak acid, the atria can be lifted from the ventricles, thus exposing the atrio-ventricular rings, which are of fundamental importance for a proper understanding of the structure and function of the heart. In other words they are the tendons of origin of the bands of heart-muscle. Dr. Mall saw that this discovery reopened the subject of the architecture of the heart; and that here was a point where progress could be made. In 1900 he gave to John Bruce MacCallum the study of the bands of the heart-muscle. MacCallum unraveled the ventricles of the heart in the embryo pig into superficial and deep spiral bands with their origin and insertion in two tendons, the atrio-ventricular rings and the chordæ tendineæ. As a tribute to this brilliant work, Dr. Mall completed the study on the adult human heart after MacCallum's death, reducing the problem to the following simple terms: To understand the beat of the heart one must figure out how a muscular bag is constructed so as to empty itself. We have Dr. Mall's specimens in the laboratory showing how the spiral cardiac bands contract with each beat of the heart in the exact familiar pattern of wringing out a rag. This prompted Dr. Mall to reconsider the development of the heart, and his work here led to what he considered the next step, that of following out the origin and development of the atrio-ventricular bundle and the Purkinje bands.

Another line of anatomical study which interested him was the study of the brain. Here he has drawn to the anthropological side. He realized that Baltimore afforded a rare opportunity to study the problem of race in connection with the brain. Dr. Hrdlička, the anthropologist in Washington, had said to him that the brain of a negro could be distinguished from that of a white man, and with this in mind Dr. Mall made a comparative study of the brains in the anatomical collection, comparing them by weights, the complexity of their convolutions, the area of the cross-section of the frontal part of the corpus callosum, and other criteria. Realizing that no man can free himself of prejudice, he charted all of his data by means of numbers, filling in the race and sex only after the charts were complete. In this way he showed that the crude present day methods are inadequate for scientific deductions regarding the relation of the brain to race and sex. Of the criteria on race there remains only the difference in the shape of the brain corresponding to the well-known difference in the shape of the head. He was profoundly interested in the subject of the development of the brain. After the monograph of His on the development of the tracts in the brain written during his last year, Dr. Mall plotted out such tracts as could be made out in the brains of his specimens, and it was, I know, one of his great desires to see this problem developed in the new Carnegie Laboratory of Embryology.

In his anatomical studies Dr. Mall has enriched his science with a wide range of methods. Our laboratory is full of examples of beautiful injections, corrosions of blood-vessels, preparations of connective tissue made by differential digestion and maceration, cleared embryos which show the development of the skeleton, and many others. Through his influence the technique of modelling has been greatly improved and extended. His own methods of work in the laboratory are of great interest, and he frequently discussed the influence of Ludwig in this connection. Contrary to the usual type, Dr. Mall was far more active mentally than physically. I have known him to think and plan with the greatest care so that a bit of routine might be simplified. Thus, it was his habit to think out every detail of an experiment before he undertook it; he never employed the system of trying a thing out without adequate preparation, or of approximating his methods through errors. For this reason he made but one experiment a day. If he failed he would not repeat it until the next day, thus giving himself ample time to think out the reasons of his failure.

He was very intolerant of the collection of unanalyzed material. His interest in technical procedures was only in their bearing upon the solving of problems; it lay in understanding the principles rather than in multiplying evidence.

We have outlined Dr. Mall's work in anatomy as it grew out of his work in Ludwig's laboratory, and we shall sum it up by saying that he approached anatomy with an interest in structure as adapted to function rather than in morphology. But he was not only an anatomist, he was also an embryologist. In 1891, he published an account of a normal human embryo, now placed in the fourth week of development. He made a most careful and accurate study of all its systems, illustrated by the surface form, in models and casts. This was the first human embryo ever modeled in America, and at that time it was the most complete account of any human embryo in existence. In this study he announced several discoveries. He described a new stage in the development of the brain and its nerves, and traced the origin of the splanchnic nerves. Here also was repeated one of Dr. Mall's earlier discoveries, namely that the Eustachian tube and middle ear arise from the first branchial arch, and in this study lay the foundation of his studies on the cœlom and the vascular system. The effect of this work on Dr. Mall is to be seen in these words in one of his publications: "I always think in human anatomy in relation

to this embryo." Huber has said that this study has served as a model for all future work of its type. It did more, for like his work on the stomach, it represents, as it were, Dr. Mall's program in embryology. Here one can see the beginning of the type of embryological work which will be associated with his name.

This specimen forms the foundation of the priceless collection of over two thousand human embryos which Dr. Mall later gave to the Department of Embryology of the Carnegie Institution of Washington. It was perfect, beautifully fixed and sectioned. When he had finished the description of it he offered it as a tribute to his teacher, His. His returned it, with several others of his own, expressing the wish that they might be the nucleus for a much larger collection. How richly has this gift borne fruit in the development of the science of embryology!

In the study of embryonic development three names stand out in logical sequence, von Baer, His, Mall. Neither His nor Dr. Mall were concerned with the phenomena of maturation, fertilization or the cleavage stages, in the development of the embryo, but the latter has characterized the work of His as laying a foundation for histogenesis. In like manner the work of Dr. Mall in normal embryology may be summed up in the term organogenesis. He has traced the growth of organs up to their adult stage. He has laid the foundation for a complete anatomical survey of the human embryo in all stages of its development. Here, for example, belong his studies on the diaphragm. Based on the discovery of His that the diaphragm arises in the head, in the septum transversum, and shifts caudalward, Dr. Mall determined the origin of the pleuro-pericardial membranes and the pillars of the diaphragm, and then traced the shifting of the diaphragm to its final position in the adult. The same type of work is seen in the study of the ventral abdominal walls, following the shifting of the rectus muscle, and still more clearly is it brought out in his study of the loops of the intestine. He followed the pattern and position of these loops, first in their early shifting from the cœlom into the cord, and subsequently studied the mechanism of their return back into the abdominal cavity as the fœtus develops. In the dissecting room he determined the normal position of the loops in the adult, and by experiments on animals showed that both the intestine and the omentum seek their normal position when disturbed. Of this work His wrote:

Your satisfaction in your work will be lasting, because you have brought light into a field which was so obscure. The thing which has been lacking in all of our studies on development up to this time has been observations on the transition between the early embryonic and fœtal stages up to the form of the adult. For the intestine you have given the entire study from the beginning up to the end, and I regard it a great step in advance.

It is in connection with the development of the vascular system that Dr. Mall made some of his most significant contributions to embryology. One of the most important points in the study of the embryo mentioned above was solving the problem of the primitive ventral branches of the aorta. This he did by showing that the vessels which are the forerunners of the cœliac axis and superior mesenteric artery arise as far forward as the first dorsal segment, and by indicating the method by which they shift back to their position in the adult. This work has since been repeated with more specimens but not analyzed with more insight. I recall in connection with these more elaborate subsequent studies on this subject one of Dr. Mall's characteristic comments: "I can never become interested in the mere collection of new examples after a principle has once been thoroughly established." It is in his work on the development of the vascular system that his physiological bent and the theories he entertained concerning growth gradually converge. He saw the fundamental significance of endothelium in connection with the vascular system; that blood vessels are not parts of the great system of tissue-spaces, with their slow movement of the fluid contained, but are determined rather by a special smooth lining of a differentiated cell or endothelium. He carried over to embryology the methods of injection of blood-vessels and lymphatics in use for the adult and thereby made possible the study of the spread of vessels in the embryo of his own work and that of his students, as illustrated in the Manual of Human Embryology, edited by Keibel and Mall. There is represented the progress which was made by the laboratory under his guidance. He established the method by which it will be possible to give a complete account of the development of the vascular system.

Dr. Mall also discovered the fact, now abundantly confirmed, that endothelium can give rise to the fibers of reticulum. In the study of the vascular system he emphasized again and again the value of the study of the organ as a whole. Trained by the man who invented the microtome and himself making improvements on it, he reacted strongly against those anatomists who study only sections. He was interested in the architecture of an organ; to use one of his own phrases he had "a feeling for a structure." Indeed he has often said that if he were to choose a career again, it would be that of an architect. His gift in anatomy, like the gift of a sculptor or the architect, was the power to visualize structure in three dimensions. Thus one can understand his pleasure in the studies of the architecture of the vessels of organs, given not in indefinite terms but showing the exact pattern of all the vessels, the number and relation, the order of arteries from the main to the terminal branches. Thus he has left to us a rich heritage of corrosions of all of the arteries and veins of various organs which is worthy of a place in the great scientific museums of the world. In the study of the development of the vascular system he, more than any one else, has analyzed the laws of vascular growth as outlined by Thoma.

During the latter part of his life, Dr. Mall became more and more interested in the problems associated with his collection; that is to say, in the type of problems for which institutes for research are founded, and which depend for their solution upon the analysis of a large amount of material and the cooperation of experts along closely allied lines. These problems touch more and more closely the problems of clinical medicine and social welfare. Such, for example, is the study of abnormal embryos, leading up to the analysis of their fre-

quency and causes, the study of tubal pregnancy, the normal curve of growth for the human embryo, the determination of its age, the nature of implantation, and the causes of sterility and abortion. He first became interested in the study of abnormal embryos through separating the normal from the abnormal in his collection. In 1893 he described a specimen, then the youngest in his collection, as a normal embryo of the second week, and later concluded that it was an older abnormal embryo. His first general account of abnormal embryos was in the volume of The Johns Hopkins Hospital Reports, published in honor of Dr. Welch in 1900. Eight years later he published a monograph on monsters of which Morgan wrote:

The recent publication by Mall on the causes underlying the origin of human monsters marks an epoch in the study of teratology in this country, for he has treated the subject with a breadth of view and a wealth of illustrations rarely found in the handling of this complex question. Mall has brought to the task a profound knowledge of the older literature of the subject, an appreciation of the most modern results in experimental teratology, and a thorough familiarity at first hand with the subject of human monsters. The physician and anatomist are brought into close touch with the work generally supposed to be outside their proper field; and on the other hand the student of malformations in the lower animals will be made to appreciate the inexhaustible supply of human materials with which the anatomist and physician are familiar.

In this study and in the work of the last six years, Dr. Mall has given a masterly analysis of the causes of monsters. He has shown that from the earliest ages of the world's history the study of monsters has been one of the capital problems of anatomy, medicine and natural history; that the belief in supernatural causes gave way to the theory of maternal impressions, and that this must now give way to a scientific analysis of their causes. Dr. Mall recognized that a few abnormalities, polydactyly for example, are germinal and cannot be produced experimentally; but that monsters are not due to germinal or hereditary causes, but are produced from normal embryos by influences which are to be sought in their environment. The cause of monsters, he has indicated, lies buried in the non-committal term of *faulty implantation*. Thus the study of normal and abnormal implantation of the embryo became one of the chief problems which he proposed to study in the new institute of embryology. In his recent paper on cyclopia he has given a masterly analysis of the recent work in experimental embryology. He showed that as soon as Stockard succeeded in experimenting with eggs in such a way as to produce cyclopean monsters at will, the explanation of the process was at hand; for the work demonstrated that a slight change in chemical environment, acting at a critical time, caused cyclopia. Dr. Mall studied the cyclopean monsters in his collection, one of which is at a stage where a complete analysis could be made, and in conclusion he says: "It seems to me that the studies based upon our collection of embryos, as well as recent investigations in experimental embryology set at rest for all time the question of the causation of monsters. It has been my aim to demonstrate that the embryos found in pathological human ova and those obtained experimentally in animals are not analogous or similar, but identical. A double monster or a cyclopean fish is identical with the same condition in human beings. In all cases monsters are produced by external causes acting upon the ovum." Thus, most localized abnormalities and monsters, of which he gives a wealth of illustrations, can be traced back to the faulty nutrition of the embryo at early critical stages, and the effects can be followed with every grade of intensity, from complete degeneration of the ovum to monsters which survive to term. One of his most interesting deductions is that in some forms of faulty implantation there results dissociation of the tissues of the embryo, so that they grow exactly as do the cells in experiments with tissue-culture, without the correlating forces which check and integrate the organs in normal development.

It is to my mind a significant example that this work was carried on during the years given to the organization of a new department, that the work of administration was so planned that it did not check research. It is not too much to say that this work of Dr. Mall opens up a whole new field, and that it has already formed a broad foundation on which all future study of abnormalities in development must rest. Such was the work with which he was engaged at the time of his death. In his vision of an institute for embryological research he saw that two great lines of work in which he was most interested could be brought to a successful conclusion within a reasonable limit of time. First, that the full development of the study of organogenesis could give us a completely rationalized anatomy, and that only by completing the story of the development of the organism could we hope to understand its normal structure and its range of variation. Second, that there is a group of problems such as determination of the curve of growth, the study of abnormalities and their causes, normal and abnormal implantation and others which may be grouped together under the study of the laws of growth which lie beyond the powers of a single individual, and are thus only to be attacked through organized research. How often has he said during the latter months of his life, "my work is mapped out for the next ten years." Fortunately in his "plea for an institute of human embryology," and in some unpublished manuscripts some of these plans are recorded, but for the loss of those coming years that would have given us his greatest achievements, those achievements for which his whole life has been the preparation, no philosophy can console us. About a month before his death he put the question to me: "What would you say had been the effect of the Carnegie Institute of Embryology upon this laboratory?" to which I replied: "It has lifted the research of the place from a somewhat amateurish state to a professional state." Never shall I forget the pleasure in his face as he replied, "it is exactly what I wished to do." Such was his aim, such the ideal from which he had never swerved from the very beginning of his career.

No account of Dr. Mall's scientific work is complete without a mention of his contribution in the training of others. It is well known that Ludwig published but little under his own

name, so that as time goes on most of his ideas will live through the works of those he trained. Dr. Mall has done both; what he himself accomplished has just been only briefly recorded from a study of something over a hundred works from his pen. Besides this he has developed in this country what might be termed a school of anatomy, represented by five hundred articles which have appeared from his laboratory. Of teaching he had the highest ideal. He once said, "What higher title could there be than that of a great teacher?" That he himself was one of the world's great teachers will be realized when his influence in the development of medical education in this country is adequately analyzed. To the general problems of education he gave deep thought and great originality. His teaching was characterized by two broad principles, which were followed in his own laboratory: First, that each student should approach his work in the spirit of a discoverer. Second, that since in each class there may be those who are destined to become the intellectual leaders of the next generation, liberty in education is absolutely essential, in order that the strong personality might develop. His own methods of training others were unique—so bound up with his own rare personality that none could copy, and few describe them. He had a gift, perhaps a genius, for stimulating thought. Rarely, indeed, by question; the quiz he never used; it was more in the nature of an occasional suggestion, the acuteness of which impressed one more and more profoundly as one pondered over it. Perhaps his most fundamental quality was his rare generosity which, I am convinced, he would freely ascribe to the influence of Ludwig. I recall distinctly an instance in which a student had worked carefully and accurately with him without, however, understanding the meaning of the value of his observations. The student became discouraged and had decided to give up the work, when Dr. Mall asked for his notes, and later published a very interesting paper under the student's name. This incident is most interesting in connection with one of Dr. Mall's letters, written in the early days of the medical school when he was homesick for the laboratory of Leipzig. He cites therein that before leaving Leipzig he had given some incomplete studies to Ludwig evidently expecting him to use them in his own work, but that Ludwig had added experiments and published them all under Dr. Mall's name. He then concludes: "Can you blame anyone for wanting to return to one who would do things like that?" Ludwig, he wrote, was entirely without selfishness, and when I tried to thank him for all he had done Ludwig replied, "Pass it on." This, indeed, became the great watchword of Dr. Mall's life. Most freely did he give his ideas and his energies to his students. You will find no joint research with his students because all that he gave them he meant to be theirs. He demanded in return the development of high standards of work. In fact, perhaps the most lasting effect which he made upon the minds of his followers was the value of scientific standards and the meaning of ideals in research. He never gave first hand praise; the only encouragement which a pupil received was a genuine interest in his work, but what a rare enjoyment when the teacher discussed with the student his preparation. He made the rounds of the laboratory nearly every day and gave his staff and his students much of his time. Each one learned that Dr. Mall was sure to come while he was making progress to enjoy it with him, and thus the student came to find enjoyment where Dr. Mall found his—in the work itself. Many of his informal talks in the laboratory were on general topics rather than on the specific development of research, and so general, often so whimsical were these discussions that their meaning was lost entirely upon more than one student.

In the organization of departments there are leaders who train others only in their own problems, giving little scope for independent work. Dr. Mall, on the contrary, was keen to give opportunities to those who could develop an independent line of research. Thus, for example, in his laboratory developed the method of tissue-culture. Again, though his own work did not lead him into the newer fields of cytology, he saw to it that this work was represented in the laboratory. An even more striking example, perhaps, is that he was the first to see that the methods of anthropology might be applied with great value to the study of embryology, hence he brought into the department of embryology professional anthropologists, thereby widening the scope of the science of embryology.

Closely bound up with his own scientific achievements is the part he played in the development of scientific publications in this country. According to his own account, when he started out he hoped that the excellent *Journal of Morphology* would care for all the more complete publications of the laboratory, but it became hampered financially and finally suspended publication in 1903. During a term of years those in the laboratory well remember that he constantly discussed the feasibility of establishing a new journal. At the meeting of anatomists held in Baltimore, in 1900, a committee was formed to launch the *American Journal of Anatomy,* and its first number appeared the following November, 1901. In 1906 followed the *Anatomical Record,* both published first in Baltimore. In 1908, when the *Journal of Morphology* was resumed by the Wistar Institute, Dr. Mall's work on monsters comprised its first number. In carrying out his ideas, however, he worked through others to such an extent that many failed to realize whose was the real directing force. His originality, far-seeing vision and courage for undertaking new enterprises could not be better illustrated than in these journals. More striking still, as a sign of his ideal of developing scientific publications in this country are the new contributions to embryology, published by the Carnegie Institution of Washington.

In his introduction to the article on His, Dr. Mall wrote these words:

The ancient science of anatomy has been perpetuated during many centuries by great men who have dedicated their lives to it. The list is a long one, for the development of the science has been slow and progressive from the earliest ages to the present time; we find in it, on the one hand, some of the names of the greatest who have ever lived—Aristotle, Vesalius—on the other, the names of those who rank as leaders of a generation, Bichat, His.

With Bichat and His belongs the name of Mall. His name will be associated with the present strongly physiological bent of modern anatomy, with the laying of a broad foundation of organogenisis in embryology, whereby anatomy is being rationalized, and with the vision of a broadening of the scope of embryology so as to bring it into relation with the problems of clinical medicine and social welfare. In America his place is unique, it goes without saying that he was our greatest anatomist. More than any other man in American medicine he has led his generation into the way of research.

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FRANKLIN PAINE MALL, A. M., M. D., LL. D.,

Late Professor of Anatomy, Johns Hopkins University

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100. On the frequency of localized anomalies in human embryos and infants at birth. Amer. Jour. Anat., XXII, 1917, 49-72.

101. Annual Report of the Director of the Department of Embryology. Year Book No. 16 of the Carnegie Institution of Washington. (In press.) Wash.

102. On the age of human embryos. Amer. Jour. Anat., 1918, XXIII, 397-422.

103. With Dr. A. W. Meyer. (In preparation.) A survey of and studies on pathological ova in the Carnegie Embryological Collection. To be published in "Contributions to Embryology."

104. With Dr. J. W. Williams. (In preparation.) Implantation of the human ovum. To be published in "Contributions to Embryology."

SEPARATE MONOGRAPHS REPRINTED FROM THE JOHNS HOPKINS HOSPITAL REPORTS.

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IN MEMORIAM

EDWIN S. LINTON

Edwin S. Linton, a member of the class of 1918 of The Johns Hopkins Medical School, died in France on November 4, 1917. He was a son of Professor and Mrs. Edwin Linton, of Washington and Jefferson College, and a native of Pennsylvania. He graduated at Washington and Jefferson College in 1913 and, after a year of post-graduate study at the same institution, entered The Johns Hopkins Medical School in 1914, where he was an earnest and enthusiastic student until he became a member of The Johns Hopkins Hospital Unit and went to France. At first he was assigned to service at a port hospital for two months as a night superintendent, an admitting officer in the out-patient department, and in the operating room.

Later, he rejoined the staff of the base hospital. After serving in various capacities, he finally was assigned to the medical service as an acting interne.

Upon November 10, 1917, he fell ill with scarlet fever and died, four days later. His death was felt keenly by all, and especially by his classmates and associates, with whom he was a great favorite by reason of his ready wit and optimistic temperament.

Flowers were sent by officers, nurses and fellow students. He was laid to rest on November 15, 1917, with full military honors in the little French cemetery near Base Hospital No. 18.

LYLE BARNES RICH

Lyle Barnes Rich, a member of the class of 1918 of The Johns Hopkins Medical School, died of disease on December 8, 1917, at Base Hospital No. 18, American Expeditionary Force, France, in his 26th year. He was one of a group of 34 medical students who went to France in the summer of 1917 in connection with The Johns Hopkins Hospital Unit.

He was a native of Minnesota, a graduate of the University of North Dakota, and a student at The Johns Hopkins Medical School since 1914. He was an excellent student, being thorough and painstaking in all his work. Although quiet and reserved by nature, he was a sympathetic friend and wise counsellor to such as were in need of advice or assistance. He had an intuitive knowledge of human nature and a keen perception of character. He was fond of reading, of poetry, and also of music. He was a church member and a consistent Christian.

While in France, he was for the most part assigned to laboratory work, largely in blood determinations and serum reactions, and proved himself to be a careful, painstaking and reliable observer. He was buried in the little hospital cemetery in France with military honors, attended by the whole personnel of the Unit, by the side of his classmate, Edwin S. Linton.

MIRIAM E. KNOWLES

Miriam E. Knowles, daughter of Mr. and Mrs. Thomas C. Knowles, of Yardley, Pennsylvania, died November 12, 1917, at Base Hospital No. 18, American Expeditionary Force, of scarlet fever, after an illness of five days.

Miss Knowles was a graduate of Wellesley College and of The Johns Hopkins Hospital Training School for Nurses, class of 1916. She was an enthusiastic member of The Johns Hopkins Unit, interested in her work, and devoted to her patients; and they to her. Each day in her round of duties, she seemed to find another reason why she was glad to be considered among the first on duty in France, ready to serve her country.

She was buried with other Americans in a little French cemetery very near Base Hospital No. 18. Simple, but impressive, ceremonies were conducted by a clergyman connected with the Y. M. C. A. "Lead Kindly Light," the most loved of hymns, was beautifully sung by a quartette of medical students. The nurses attended in Red Cross uniforms. The officers acted as pallbearers, with the entire personnel as escort. Her casket was draped with the American flag. There were many floral offerings from nurses, officers, students, and her friends among the patients. Every possible honor was shown her as she was laid to rest by those who had learned to know and appreciate her for what she was—a loyal friend and a devoted, conscientious nurse, who had given her life for her country.

NEW PUBLICATIONS.

The following six monographs:

Free Thrombi and Ball-Thrombi in the Heart. By J. H. Hewitt, M. D. 82 pages. Price, $1.00.

Benzol as a Leucotoxin. By Laurence Selling, M. D. 60 pages. Price, $1.00.

Primary Carcinoma of the Liver. By M. C. Winternitz, M. D. 42 pages. Price, 75 cents.

The Statistical Experience Data of The Johns Hopkins Hospital, Baltimore, Md., 1892-1911. By Frederick L. Hoffman, LL.D., F.S.S. 161 pages. Price, $2.00.

The Origin and Development of the Lymphatic System. By Florence R. Sabin. 94 pages. Price, $2.00.

The Nuclei Tuberis Laterales and the So-called Ganglion Opticum Basale. By Edward F. Malone, M. D. Price, $1.50.

are now on sale by The Johns Hopkins Press, Baltimore. Other monographs will appear from time to time.

NOTES ON NEW BOOKS.

The Pathology of Tumors. By E. H. KETTLE, M. D., B. S., Lond. Cloth $3.00. (*New York: Paul B. Hoeber, 1916.*)

This small volume will be appreciated by the student of microscopic surgical pathology who may easily, to say the least, be perplexed by the mass of diverse, uncorrelated nomenclature which abounds concerning tumor pathology. Adoption of the older nomenclature seems not unwise, since a knowledge of synonyms cannot be avoided and the older terms may better be learned first.

The number and quality of the microscopic illustrations in themselves make the book desirable and valuable; whereas its brevity does not bar its usefulness as a handy volume of reference. Its avowed almost total abstinence from reference is regrettable. The value to the student of such a book, in which some concrete idea of the structure of almost any given tumor is quickly to be visualized, would certainly be greatly enhanced if there were present a list of the related noteworthy publications. The scope of such a book as this can only be to furnish nuclei for more complete units of information. The fact, as the author notes, that Durante first enunciated the theory of embryonic rests, usually attributed without qualification in this country to Cohnheim, would be made of more interest to the student if the reference were at hand. This is a less vital instance of the failure of this time-saving plan of little or no bibliography.

The management of the subject matter is simple. In the first part is placed a summary of the various phases of the general biology of tumors; next the general, and thirdly the special pathology of tumors receives attention. The description is clear and concise. However, the notice given certain glands, for instance, the pituitary, is far too scanty. The book fills a niche in the domain of *surgical* or *tumor pathology* reference books, although its limitations are easily seen. Not the least of the latter is its almost total omission of macroscopic considerations. It is, however, an efficient presentation of many of the "chief points" of microscopic tumor pathology, and should be a handy book for every second and third year student. W. C. D.

Finch and Baines: A Seventeenth Century Friendship. By ARCHIBALD MALLOCH, B. A. (Queens); M. D. (McGill); Temporary Captain, Canadian Army Medical Corps. (*Cambridge: At the University Press, 1917.*)

This charmingly written and beautifully printed quarto of 89 pages, with 9 full-page photogravure illustrations, owes its inception, if we are to credit the author, to the suggestion of Sir William Osler, who has given such an impetus to medical biographical studies in America and England. The lapse of years does not render it difficult for the writer of this brief review to remember "Archie Malloch" as a boy under surgical treatment at The Johns Hopkins Hospital, and to recall his acute mind and his keen interest in the better forms of literature. It is not strange that in after years he should have developed a fondness for the studies which have given us this volume.

The Seventeenth Century Friendship relates the story of the intimacy between Sir John Finch (1626-1682) and Sir Thomas Baines (1622 or 24-1680). Both were medical men and graduates of Cambridge University, which in the troublous times of the period seems to have been preferable to Oxford as a place of study. Both journeyed to Italy together and spent some years at Padua and received degrees there. They later resided at Pisa, where Finch occupied the Chair of Anatomy in the university there under the patronage of the Grand Duke of Tuscany, and remained several years. He had as associates such men as Malpighi, Steno, Borelli and other famous names. Upon Finch's return to England he was made a physician to the Queen, was knighted by Charles II in 1661, and later sent as an ambassador to the Duke of Tuscany. His friend Baines was also subsequently knighted, and appointed a professor of music at Gresham College. Both Finch and Baines were among the original charter members of the Royal Society of England.

Notwithstanding a decided scientific attitude of mind towards natural phenomena, Finch was not always free from a certain amount of unscientific credulity. He believed that on one occasion a shower of wheat occurred in Italy, and also that the pictures on the walls of a church on certain feast days descended from the walls of their own motion. He also became interested in the case of a blind man in Holland who claimed to have the ability to detect color by touch. Finch seems to have had a degree of incredulity about him, but does not avow his utter disbelief in the possession of such power. The friendship of Finch and Baines seems to have been most intimate. Baines accompanied Finch to Constantinople when the latter was made ambassador, and died there; his remains were brought to England by Finch on his return.

Finch never married, it is thought, out of consideration for the wishes of Baines. The friendship between the two was most cordial and each seems to have supplemented the qualities of the other. Neither were great physicians or investigators, but both were interested in studies which were common to medical men at those times. They were eager for curious bits of natural history and semi-scientific knowledge. Finch seems to have been the best anatomist and man of science; Baines, on the other hand, was the better philosopher and broader thinker. The letters so freely printed which passed between Finch and his sister, Anna Conway, and other relatives threw much light upon contemporary history, manners and customs. The volume also shows the debt of English medical study, especially in anatomy and chemistry, to Italy in the 17th century. The author deserves great praise for the painstaking and admirable use which he has made of his materials.

H.

A Text-Book of Nervous Diseases for Students and Practising Physicians. In thirty lectures. By ROBERT BING. Translated by CHARLES L. ALLEN. Cloth. (*New York: Rebman Company, 1915.*)

As the translator states in his preface, this is a thoroughly useful, practical and up-to-date book. Both the student and the practitioner should find it so. In size between the summary compends and the larger handbooks, it is convenient to handle, the type is good and the illustrations are excellent.

The subject matter is well arranged and well presented. It would be even more attractive had the translator followed less closely the original German phraseology.

The nervous manifestations of arteriosclerosis are especially well treated. T. P. S.

Diseases of Occupation and Vocational Hygiene. Edited by GEORGE M. KOBER, M. D., and WILLIAM C. HANSON, M. D., with illustrations and reference tables. Cloth $8.00. (*Philadelphia: P. Blakiston's Son & Co., 1916.*)

No one connected with an active out-patient clinic in a large manufacturing community can fail to be impressed with the frequency with which occupational diseases are met with, owing to the fact that very often adequate protective measures are not instituted in many manufacturing establishments. Fortunately, the more enlightened manufacturers are gradually becoming alive to the importance of protecting their workmen against intoxications of various kinds, partly from humanitarian motives and partly owing to the fact that failure to do so has taught them that they lessen the industrial efficiency of their employees. This volume

is, therefore, very timely, since it brings up to date the knowledge that has been acquired concerning the various occupational diseases, as well as the best measures for preventing them. No dispensary, public health official, social worker, corporation surgeon, or director of a manufacturing plant, where the health of its employees is endangered, should be without this modern treatise.

The editors, the senior member of whom has done so much for the furtherance of industrial hygiene in this country, in a prefatory note, give a most interesting historical account of what has been done up to the present time towards preventing industrial diseases among workmen engaged in menacing occupations. England was the pioneer nation to grapple with this important problem, followed by France, Germany and the United States. Much useful legislation has been enacted in these countries to lessen the menace from various dangerous trades.

The work is really a collection of monographs by specialists in their particular lines. The authors are John B. Andrews, Irene O. Andrews, George L. Applebach, Bailey K. Ashford, Clarence J. Blake, John T. Bowen, Louis Casamajor, C. H. Crownhart, Luigi Devoto, Seward Erdman, Langdon Frothingham, Alice Hamilton, Emery Hayhurst, Charles R. Henderson, Frederick L. Hoffman, Frederick S. Lee, Thomas S. Lee, Thomas M. Legge, Harry Lilienthal, Owen R. Lovejoy, Sir Thomas Oliver, Thomas Ordway, Harry C. Soloman, Elmer E. Southard, Ludwig Teleky, John W. Trask, Ernest E. Tyzzer, George C. Whipple and H. V. Würdemann.

The editors have divided the subject matter into three parts.

Part I deals with the specific and systemic diseases of occupation, including fatigue and the neuroses.

Part II deals with the causation and prevention of occupational diseases and accidents.

Part III is intended to be of service to those who may be called upon to investigate in the shop or factory, and in the dispensary and hospital, the relations of occupation to disability and disease.

For two decades Thomas Oliver's "Dangerous Trades; The Historical, Social and Legal Aspects of Industrial Occupations as Affecting Health" has served a most useful purpose as a work of reference. The present work, to which Sir Thomas Oliver is a contributor, brings our knowledge of occupational diseases thoroughly up to date. T. B. F.

Some Personal Reminiscences of Dr. Janeway. By James Bayard Clark, M. D. (*New York: G. P. Putnam's Sons, 1917.*)

This tribute to the late Dr. E. G. Janeway by an intimate friend is marked by a sincere desire on the part of the author to portray him as he knew him in his daily life in contact with patients and students, and in his professional studies and public life. Dr. Clark gives many interesting reminiscences of acts of kindness towards the sick and deserving, and anecdotes of a personal character showing Dr. Janeway's manner of life and modes of thought. He was kind in his relations with young and inexperienced physicians; he loved his profession, and was high-minded in the performance of all duties; he strove to advance the science of medicine by his labors and studies. The gratitude of the author to Dr. Janeway is most creditable, and forms in reality the key-note of the little book.

The Obstetrical Quiz for Nurses. By Hilda Elizabeth Carlson. Cloth $1.75. (*New York: Rebman Company, 1915.*)

In writing this "monograph on obstetrics" the author has placed before pupil nurses the first obstetrical quiz compend written for their special needs. For some time the necessity for such a book has been apparent and this work is an excellent attempt to supply this need. In the instructive question and answer form it covers the essentials of obstetrical anatomy, physiology, and pathology. A very good feature is the attention given to the proper methods in emergencies arising in obstetrical practice at homes.

The chapters on anatomy, physiology, and normal labor are especially well written and the lists of supplies given in Chapter VI should prove of great value to nurses undertaking the care of obstetrical patients at home. The chapter on the new-born child is valuable, as the average nurse knows far too little about the less important of her two patients.

There are a few undesirable features about the book. The advice to nurses to attempt replacing a prolapsed cord by intravaginal manipulations is not good. The two last chapters on anæsthesia seem uncalled for and out of place in the book and it is to be hoped that they will be omitted from future editions. The first of these on scopolamine-morphine anæthesia is admittedly a copy of the report of Rongy and Arluck published in the New York Medical Journal in September, 1914, and its presence in this book will doubtless be of assistance in the propaganda for "twilight sleep," a procedure that has been given up almost entirely. The last chapter on nitrous oxide anæthesia is compiled from the reports of several men and is the poorest part of the book.

Although a casual reader may think this book too voluminous and condemn it because of much detailed matter, it is this very attention to minutiæ that should make the obstetrical quiz of invaluable assistance to the obstetrical nurse. J. G. M., Jr.

Operations on the Bones, Joints, Muscles and Tendons. By Robert Soutter, M. D. Cloth $4.50. (*New York: The Macmillan Company, 1917.*)

This book considers the various orthopædic procedures, regionally, in a very satisfactory way. The methods outlined are given completely and in great detail. The cuts are diagrammatic and clear, not handicapped by any attempt at artistic display. The book is extremely well gotten up for the "occasional orthopædist."

Certain general procedures are repeated in detail each time reference is made to them, as in arthroplasty, overlapping fractures, methods of drainage, etc. This seems unessential.

There seems to be too much emphasis laid on the use of silk as tendon extensions in muscle transplantations, as, for instance, at the knee, where the hamstrings may be anchored directly to the patella, avoiding the complicated technique of silk extension to the patella and tibia. I. Z.

Embryology, Anatomy, and Diseases of the Umbilicus, Together with Diseases of the Urachus. By Thomas Stephen Cullen, Associate Professor of Gynecology in The Johns Hopkins University and Assistant Visiting Gynecologist to The Johns Hopkins Hospital. Illustrated by Max Brödel. (*Philadelphia and London: W. B. Saunders Company, 1916.*)

The delay in giving an earlier review of this monumental work, due to unforeseen, regrettable and irremediable accidents, renders a fresh detailed review unnecessary now. The book bears lasting testimony to the ability, scientific zeal and great industry of the author, who has performed his self-appointed task so well that one feels that the same intensive work will never need to be done again. The volume is an exhaustive presentation of a group of hitherto obscure diseases, and contains 680 pages with 269 figures in the text and 7 full-page illustrations.

It seems, however, to the reviewer a fitting time to add for the benefit of the readers of the Bulletin, many of whom are especially interested in the work and its author, extracts from some of the reviews which have appeared elsewhere, as showing the reception accorded to it by surgeons and pathologists.

The *Lancet*, London, says: "This book, however, deals not only very fully with all the known diseases of the navel, but also with such other matters as the omphalomesenteric duct and vessels, Meckel's diverticulum, and the urachus. The importance of

the embryology of the umbilicus is very considerable because so many of the lesions are due to a partial or complete lack of closure of the omphalomesenteric duct or of the urachus. The section devoted to this subject is extremely clear, and is illustrated by a very fine series of drawings by Max Brödel. The many interesting and instructive points which a detailed study of the anatomy reveals are well set out in Capter II, and the four plates showing the different forms of the umbilicus will be a revelation to those who have never studied this region particularly. Umbilical infections and hemorrhage in the new-born child happily have lost the importance they once had, but an account of many of the old epidemics is given by the author and their relation to infections of the umbilical stump clearly shown. A large number of cases of the curious tumors, formed by remnants of the omphalomesenteric duct, the so-called umbilical polyp, are collected and given in full, while the chapters dealing with a patent omphalomesenteric duct and prolapse of the bowel through such a duct are most interesting. As the author rightly points out, when a small umbilical polyp is noted after the cord has come away, the probable persistence of other portions of the omphalomesenteric duct, such as a Meckel's diverticulum or a cord from the mesentery to the umbilicus, must be remembered, and the added possibility of intestinal obstruction developing later in life explained to the parents. It is interesting to find that most of the cases of so-called dermoids of the umbilicus turn out on further investigation to be nothing more than inflammation due to the irritation of an umbilical concretion, the presence of caseous material and wool from the patient's clothing having led to an erroneous diagnosis in many of the cases. Records of cases of Paget's disease, diphtheria and syphilis of the umbilicus are given, and also numerous cases illustrative of the escape of intra- and extra-abdominal fluid, mostly pus, through the umbilicus as well as cases of umbilical fistulæ.

"Among the most curious of all the conditions described is the series collected by Dr. Cullen of umbilical tumors containing uterine mucosa or remnants of Müller's duct, in reality adenomyomata of the umbilicus. It was a case of carcinoma of the umbilicus which first led the author to a study of the whole subject, and the chapter on that condition contains the records of many cases of both primary and secondary carcinoma of this region."

The *Edinburgh Medical Journal* says: "The author confesses that up till the year 1904 he had thought that hernia was practically the only lesion to be noted in this locality. A chance case of cancer of the umbilicus, which he happened to meet with in his practice, sent him to the library in search of any records extant of a similar condition. He was astonished at the wealth of material on the umbilicus which he found scattered throughout the literature of surgery, and decided to collect and analyze it. The result of his labors astonishes us. His investigation has been most thoroughly done—the mere assembling of the literature to the end of 1912 took three years—and, with the aid of a number of collaborators, he has summarized what had been written up to that date so completely that no one need go further than his pages to find the gist of what has previously been written on the subject.

"With the aid of a series of excellent diagrams made by Max Brödel the description of the embryology of the umbilical region is rendered perfectly clear, and the understanding of the various congenital defects that are later described is greatly facilitated. The section on the anatomy of the umbilicus is illustrated by four plates containing 60 drawings of 'normal umbilici,' no two of which bear more than a superficial resemblance to one another. In fact, the differences are so marked that it is difficult to conceive a normal type. The author, indeed, has had to divide them into no fewer than nine groups.

"A chapter is devoted to umbilical infections in the new-born, each form of infection being illustrated with notes of a few typical cases. Umbilical hemorrhage is dealt with in a most instructive and useful way. The numerous conditions associated with aberrations of the omphalomesenteric duct are fully described and profusely illustrated, as are also those of urachal abnormalities. Among other chapters of real clinical value are those on umbilical concretions, tumors and infective granulomata.

"As we have already indicated, this work represents an enormous amount of literary research, as well as pathological and clinical observation, and it forms a valuable source of reference."

The *American Journal of Obstetrics and Diseases of Women and Children* says: "It represents the result of eight years of intensive and scrupulously careful research work. The assembling of the literature of the subject alone and its critical study took all of three years, and was made possible only by the facilities of the Surgeon-General's Library at Washington. As an example of the care taken in its production, when the book was set up in galley, the author, realizing that the tremendous number of cases mentioned would be most valuable with the fewest chances of error, had the entire book checked off with the original articles. Subsequent writers can accordingly feel safe in relying on the accuracy of the cases recorded."

The *Boston Medical and Surgical Journal* says: "It constituted a really complete survey of the literature upon the umbilicus and urachus, with the exception of umbilical hernia, and this survey is enriched with a large amount of original observation. Three-quarters of the volume are devoted to the umbilicus, one-fourth to the urachus, and the whole profusely illustrated with 269 text-figures and 7 plates, many of them original and some colored. The work is one of the best Teutonic type of thoroughness and value, written by an American in a charming and delightful English literary style, unusual among physicians."

The *American Journal of the Medical Sciences* says: "Perhaps it is the very portliness of the volume, perhaps it is merely a habit of much writing acquired during its preparation, that inspired the author with the idea of condensing its contents into a preface of some three thousands words. We urgently counsel those who may contemplate, as we fear some hardy souls may, the perusal of the entire volume from cover to cover, to begin systematically with the preface. Then to follow the advice therein to study (not merely to admire) the illustrations of embryology; and then (but this advice is not in the preface) to lay the volume carefully away upon its shelf, to be called upon as a work of reference whenever needed—and this, we predict, will not be very often.

"The plan of the work is all inclusive; embryology, anatomy; umbilical infections in the new-born; remnants of the omphalomesenteric duct; congenital polyps; Meckel's diverticulum; intestinal cysts; umbilical concretions; purulent and fecal fistulæ at the umbilicus; umbilical herniæ; umbilical tumors; patent urachus; urachal cysts—these are but a few of the chapter headings, for the volume treats *de omnibus rebus et quibusdam aliis*. Not only are the history, the pathology, the symptoms, the diagnosis, the prognosis and the treatment of each condition given at length, but there is appended nearly to every section a long list of case abstracts, alphabetically arranged according to the author's name, which have been disinterred from former and less worthy sepulchers to be reinterred with befitting pomp and splendor in this magnificent mausoleum." H. M. H.

Bibliography of William Henry Welch, M. D., LL. D. Prepared by WALTER C. BURKET, M. D., of The Johns Hopkins University. (*Baltimore: The Johns Hopkins Press, 1917.*)

This attractive volume of 47 pages has been prepared by Dr. Burket as a part of a larger scheme to collect and publish the papers of Dr. Welch scattered throughout the medical literature of the world. This remarkable collection of titles shows how much

material is at present buried in periodicals, transactions, reprints or manuscripts which deserves publication in a collected form readily accessible to students and teachers of medicine. The preparation of this volume has involved much care and painstaking search on the part of the compiler, who deserves the thanks of all physicians for his altruistic labors. After an examination of the wealth of material to which it is an index, one feels that the publication of the larger collection ought not to be indefinitely delayed. H. M. H.

International Clinics: A Quarterly of Illustrated Clinical Lectures and Especially Prepared Original Articles on Treatment, Medicine, Surgery, Neurology, Pediatrics, Obstetrics, Gynecology, Orthopedics, Pathology, Dermatology, Ophthalmology, Otology, Rhinology, Laryngology, Hygiene, and other Topics of Interest to Students and Practitioners. By Leading Members of the Medical Profession throughout the World. Edited by H. R. M. Landis, M. D., Philadephia, U. S. A. (*Philadelphia and London: J. B. Lippincott Company.*)

Owing to the great variety of the papers in the rapidly recurring volumes of the international clinics, it is not practicable to give any review in detail of them. The papers vary, it is true, in excellence and execution, but all make special appeal to some members of the medical profession, and hence are of value. The titles mentioned below, however, will give some conception of the scope of the papers and the appeal to one reader at least.

26th Series, 1916, Volume IV.

"Insomnia as a Dread," by James J. Walsh, M. D., New York.
"Duodenal Ulcer in Infancy," by Henry F. Helmholz, M. D., Chicago, Ill.
"The Psychology of the Criminal under the Sentence of Death," by Paul E. Bowers, M. D., Michigan City, Indiana.

27th Series, Volume I.

"The Tangled Skein," by J. Madison Taylor, M. D.
"Health Efficiency of Workers Due to their Living Conditions," by H. R. M. Landis, M. D.

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"Typhoid Fever with Complications," by Lewellys F. Barker, M. D.
"Jaundice with Enlarged Liver in a Young Adult," by Thomas McCrae, M. D.
"A Group Study of the Results of One Hundred Physical and Mental Examinations of So-Called Well Children," by William R. P. Emerson, M. D.
"Skin Grafting" by Arthur M. Shipley, M. D.
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Clinical Cardiology. By Selian Neuhof, B. S., M. D. Cloth $4.00. (*New York: The Macmillan Company, 1917.*)

As its name indicates, "Clinical Cardiology" is written primarily from the clinical standpoint. The first third of the book, which deals with the anatomy and physiology of the heart, instrumental methods of examination, and the arrythmias, is concise, though this conciseness leads at times to a somewhat dogmatic treatment of controversial matters, as for instance, the description of the course of the excitation wave in the ventricle. The experimental and pathological work on which the interpretation of graphic records is based, receives scant attention. The portion dealing with the arrythmias is profusely illustrated, clear, and up to date. The passage on the displacement or hypertrophy of the heart, and the form of the electrocardiogram is excellent, and the author's views on splitting of the P and R waves are of interest. Throughout this portion of the book care is taken to correlate clinical signs with graphic records.

The chapter on orthodiascopy is much needed. Perhaps the most valuable part of the book is that on physical examination, on which are brought to bear a great many resources not commonly appreciated. The author's distrust of percussion outlines will be shared by all those who have access to the X-ray even if his "rational method" fails, because of its indirectness, to meet with favor.

The chapters on endocarditis, myocarditis and cardiac syphilis embody much valuable material, formerly accessible, if at all, only with difficulty. That on myocarditis and coronary sclerosis has the same merit and is probably as clear as the present state of our knowledge on these subjects will admit. Intraventricular conduction defects might have well been mentioned in this connection. Recent attempts at exact measurement of the cardiac reserve are dismissed in a page, as inferior to general clinical observations before and after exercise, yet at least one such measurement promises to be of value, namely, Peabody's estimation of the cardiac reserve by means of the vital capacity of the lungs. The remainder of the book is devoted to miscellaneous topics, cardiotherapy, renal tests in cardiac disease, the management of cardiac disease, blood pressure, weak heart, precordial pains, and therapy of the circulation in pneumonia.

The arrangement of the book might be improved, in spite of the difficulty caused by the variety of topics necessarily included. A fairly extensive bibliography with few important omissions is appended to each chapter, which would have been more useful but for the conspicuous lack of references to specific authors throughout the text. Those who desire a detailed knowledge of the physiology of the heart, normal and pathological, or of its pathological lesions will fare better elsewhere. Those who appreciate the work of a keen and original clinical observer on the circulation as viewed from the clinical standpoint, with sufficient description of graphic methods to make the volume intelligible, will find it both stimulating and valuable. H. B. R.

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